

**EVALUATION OF MIGRAINE DRUGS USING
MULTI-CRITERIA DECISION METHOD.**

**A THESIS SUBMITTED TO THE GRADUATE
SCHOOL OF APPLIED SCIENCES
OF
NEAR EAST UNIVERSITY**

**By
LAFI HAMIDAT**

**In Partial Fulfillment of the Requirements for
the Degree of Master of Science
in
Biomedical Engineering**

NICOSIA,

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I declare that my thesis and all the information it contains are in accordance to the academic and ethical conduct. I also declare that all articles, journals and various sources of data in relation to my thesis have been appropriately referenced and cited.

Name, Last name:

Signature:

Date

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To my Family

ABSTRACT

Migraines is a medical condition people across all spheres of life face at least every week if not every day. It may arise by various reasons such as stress, fatigue, hunger, and other medical conditions, etc. migraines can range in their severity and the location in which they occur. The migraine experience can also vary from one patient to another and maybe be due to mere stress or an indication of fever or other disturbing health conditions. There are several treatment options for migraines. However, the most popular go-to options are treatment by drugs. There are several types of drugs and brands targeted in solving migraine problems some of which include paracetamol, nadolol, timolol, botulinum toxin type metoclopramide, domperdone, pizotifen, and sumatriptan, etc. it can be a difficult struggle choosing which drug among the vast drugs and brands that best suit a specific condition of migraine relating to patient or which one under general condition such as cost of drugs, drug to drug interaction, concentration, and drug efficient, etc. is best among the alternatives.

For this reason, this thesis seeks to use fuzzy PROMETHEE, a multi-criteria decision-making technique to effectively compare 24 alternative migraine drugs that would assist medical professionals in administering effective migraine drugs in either in general situation or patient-specific situation.

Keywords: Migraines; Migraines Drugs; Prediction; fuzzy PROMETHEE; assisted therapy.

ÖZET

Migren, her gün olmasa da, yaşamın her alanında insanların en azından her hafta karşılaştıkları tıbbi bir durumdur. Stres, yorgunluk, açlık ve diğer tıbbi durumlar vb. Gibi çeşitli nedenlerle ortaya çıkabilir. Migrenlerin ciddiyetleri ve bulundukları yere göre değişebilir. Migren deneyimi aynı zamanda bir hastadan diğerine değişebilir ve sadece stres veya belirti veya ateş veya diğer rahatsız edici sağlık koşulları nedeniyle olabilir. Migren için çeşitli tedavi seçenekleri vardır. Bununla birlikte, en popüler tercihler ilaçlar tarafından yapılan tedavidir. Migren problemlerini çözmeyi hedefleyen, bazıları parasetamol, nadolol, timolol, botulinum toksin tipi metoklopramid, domperdon, pizotifen ve sumatriptan vb. Gibi çeşitli ilaç ve markalar vardır. ve hastaya ilişkin belirli bir migren koşuluna en uygun olan veya ilaç maliyeti, ilaç-ilaç etkileşimi, konsantrasyon ve ilaç etkin, vb. gibi genel şartlar altında hangisinin alternatifler arasında en iyisi olduğu markalar.

Bu nedenle, bu tez, tıp uzmanlarına genel durumdaki veya hastaya özel durumdaki etkili migren ilaçlarını kullanma konusunda yardımcı olacak 24 alternatif migren ilacını etkin bir şekilde karşılaştırmak için çok kriterli bir karar verme tekniği olan bulanık promethee'yi kullanmayı amaçlamaktadır.

Anahtar Kelimeler: Migren; Migren İlaçlar; Tahmin; bulanık promethee; yardımcı terapi.

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LIST OF ABBREVIATIONS

MRI	Magnetic Resonance Imaging
CAT	Computerized Axial Tomography
NSAIDs	Non- Steroidal Anti-Inflammatory Drugs
CABG	Coronary Artery Bypass Graft
ASA	Acetylsalicylic Acid
SSRIs	Selective Serotonin Reuptake Inhibitors
SNRIs	Serotonin- Norepinephrine Reuptake Inhibitors
MCD A	Multi-Criteria Decision Analysis
MCDM	Multi-Criteria Decision-Making
MSE	Mean Square Error
MTF	Modulation Transfer Function
OE	Origin Ensemble
OSEM	Ordered Subset Expectation Maximization
PET	Positron Emission Tomography
PROMETHEE	Preference Ranking Organization Method for Enrichment of Evaluations
RC	Resolution Compensation
SMART	Simple Multi-Attribute Rating Technique
AHP	Analytic Hierarchy Process
FBP	Filtered Back Propagation
FDA	Food and Drug Administration
CT	Computer Tomography
A.B.N	Absorption
N.O.T	Number of Tablet
CONS	Side Effect
D-D INT.	Drug-Drug Interaction
DOSE FRE.	Dose Frequency

CHAPTER 1

INTRODUCTION

1.1. Background

A lot of individuals are not able to difference between headache and migraines. There are patients who mis use the term headache for migraines and some mis use migraines for headache. Anyway, the concept and family of both these health problems are from the same root. It is ok if someone misuse these words, however, there are key differences between them. Headache is a general term use for any kind of pain around the head while migraines is a special kind of headache that may be approached differently. In order to understand the simple difference between headache and migraines, let's give a lay man's take to the definition of both terms. In a simple definition of headache, headache is characterized by an in felt pain in a region of the head either one side or both sides of the head or any particular region of the head. Its characteristics may include that it is isolated in a certain location with radiating pain from that certain location across the head.

Migraines on the other hand can be defined as a type of reoccurring headache that is throbbing by nature with the resulting impact or pain felt around one part of the head. It may be accompanied by nausea as well as disturbed vision to the patient (Mayo Clinic, 2019). The differences between headache and migraines can be further be explained in the following sentence. In a typical fashion of migraines, there is a typical feeling it comes with called the migraine aura which is a warning the human body gives as a sign that an attack is in the works. On the other hand, headache in its typical fashion do not have a warning sign (prodrome) to the human body it just occurs and it is not characterized by typical migraines characteristics such as nausea, vomiting, stomach pain, weakness or numbness. It is important to mention that despite their differences, migraines are a type of headaches and in fact the same family. Other types of headaches in figure 2 include cluster, tension, sinus, and migraine etc.

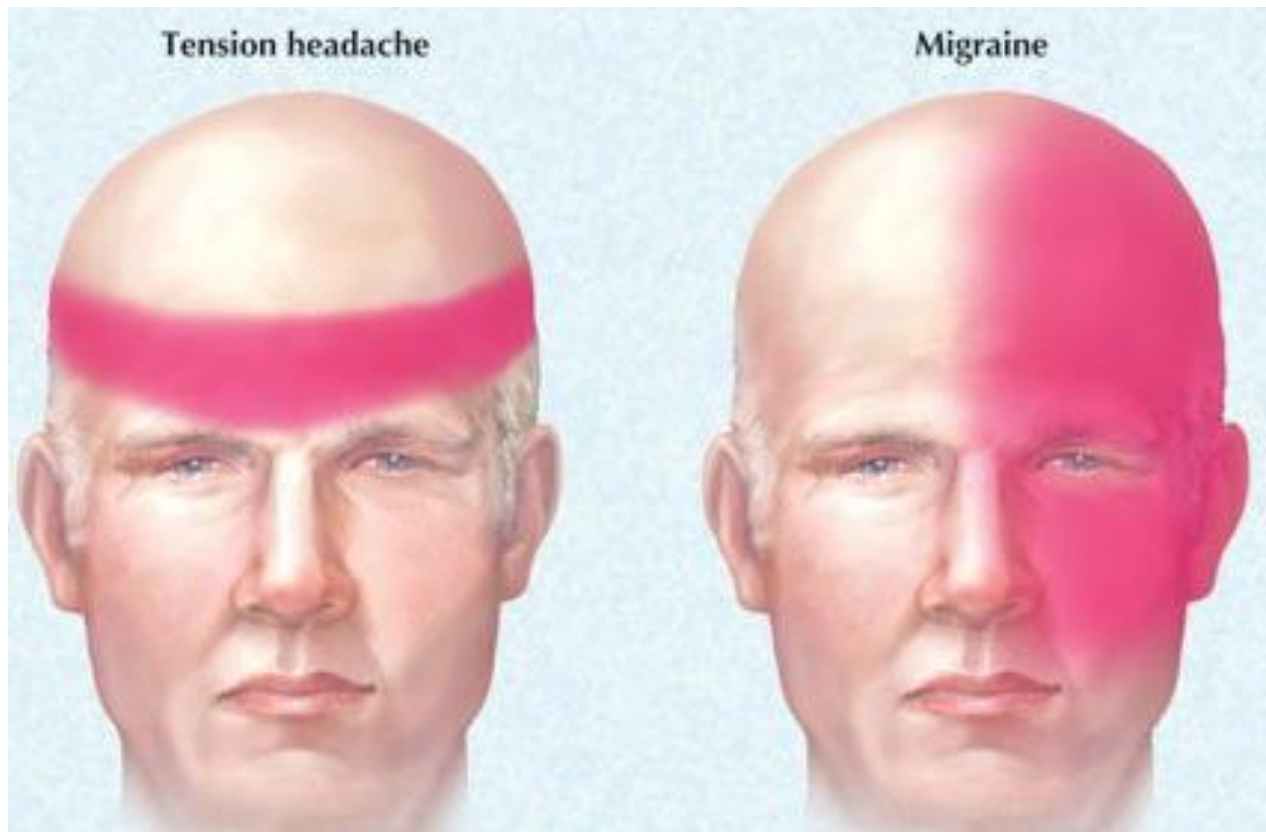


Figure 1: Difference between migraine headache

Retrieved from http://www.chiro.org/LINKS/ABSTRACTS/Prevalence_of_Neck_Pain_in_Migraine.shtml

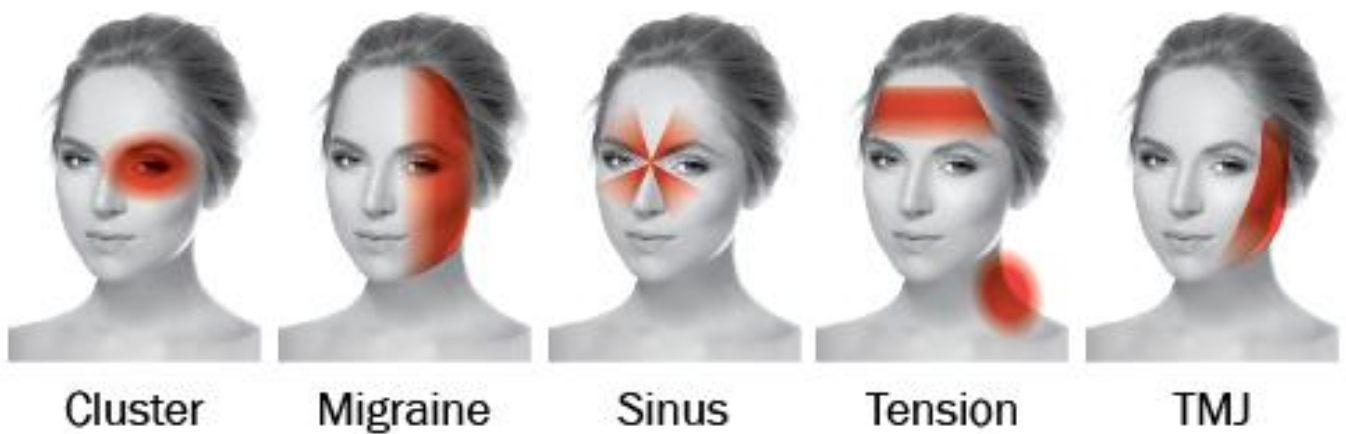


Figure 2: types of headache

Retrieved from <https://www.attainharmony.com/archives/1458>

Furthermore, it is also important to explain that migraines are more than the typical headache. Medical specialists consider it as a complex neurological health condition whose impact can

take a tool on the entire body of the patient and produce a couple of symptoms without showing any sign of headache. There are several people who basically mis diagnose migraine and confuse it for other medical health conditions. Despite several as well as ongoing research on the causes of migraines, researches have not reached a consensus regarding what actually is the cause of migraines. This is why we still have no clear diagnosis test as well as cure. If you have migraines, your medical specialist will prescribe drugs or other treatments that will help manage the condition and its symptoms so that the impact is lessen and an individual can go on with his day to day activities.

Definition and Characteristics of Migraines

Migraines can be simply defined as a type of reoccurring headache that is throbbing by nature with the resulting impact or pain felt around one part of the head. It may be accompanied by nausea as well as disturbed vision to the patient (Mayo Clinic, 2019). Migraines usually used to be described as classical/ nonclassical migraines or migraines with aura. Classical and nonclassical migraines were among the earliest terms use in describing migraines until migraines with aura recently replaced it. It is not a usual practice of specialists do not usually differentiate between migraines with aura or without aura when providing treatment. In the case of migraine without aura, specialist regards to it as a chronic headache disorder whose impact can be long lasting. It attacks on the human body can last up to 4-72 hours. When the impact of migraines exceeds more than 72 hours for a given patient, the migraine is termed Status migrainosus. Some basic characteristic of migraines includes unilateral location, moderate, moderate-to-severe, or severe intensity of the pain impacted, throbbing or pulsating nature of the pain. In some cases of migraines, there may be other characteristics such as nausea, photophobia, or phonophobia etc. migraines can be associated to genetics. According to a report, about 70% to 75% of migraine patients were discovered to have first-degree relatives who have experienced migraine before. Further characteristics found in migraine patients that are women include positive relationship with menstruation, experiencing decrease frequency during pregnancy, improve in pain during any kind of physical activities (experienced in men as well). A collection of the characteristics of migraines experienced by both men and women are provided in the next subsection.

Characteristics of Migraines:

Some of the characteristics of migraines experience by patients include;

- Impact time of migraines usually range from 4-72 hours

- The pain can range from moderate to moderate-to-severe
- There is no importance for laboratory test, the patient history will migraines can be used as an effective approach
- The attack from migraine can start at any time of the day, but it is usually experienced early in the morning
- In about $\frac{1}{2}$ of the patients, migraine is unilateral
- Humans can experience migraines 1-4 times in a month
- Gradual onset of pain, a peak for hours, slow decline
- Throbbing pain or pounding pain, pulsatile, or deep aching pain
- There are common sharp icepick jabs experienced by patients
- It is reported that between 20-35 years is the peak ages for migraines
- According to a study conducted, about 7% of males and 20% of females experience a kind of migraine in their lifetime making the ration occurrence between male and female 1:3
- There is high positive chance of getting migraines if you have family history
- Some levels of migraines are associated with nausea, photophobia, blurred vision, phonophobia, dizziness is common but not all migraines
- Some women experiencing migraines may further experience positive relationship with their menstrual period.
- Some migraine patients have also reported cold hands and or feet as well as motion sickness.

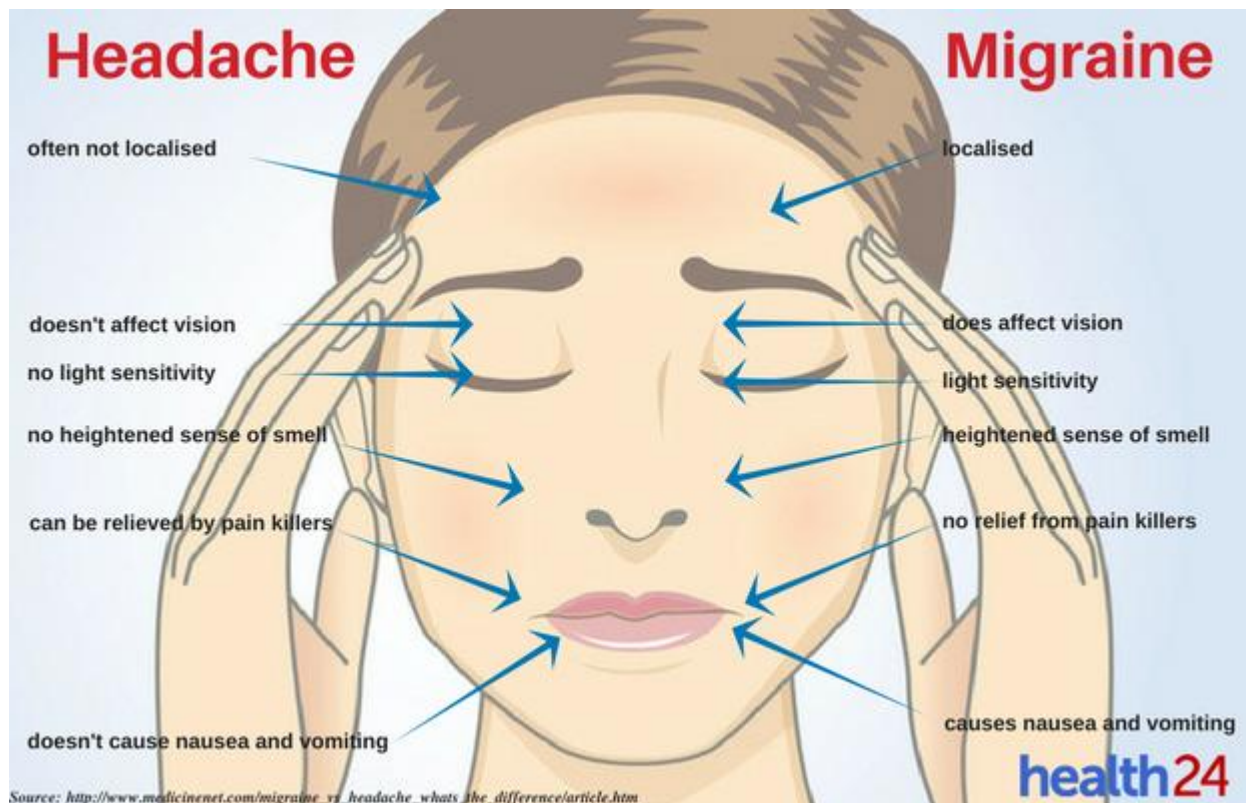


Figure 3: some of the characteristics associated to migraines

Retrieved from <https://www.health24.com/Medical/Headache-and-migraine/see-do-you-have-a-headache-or-a-migraine-20170718>

Any kind of headache that is reoccurring whether in a moderate or severe level and which is usually triggered by any of the mentioned migraine precipitating factors can be referred to as a migraine. If you remember in the previous section, we explained how migraine is a subset of headache. Some of these factors may include stress, certain foods, weather changes, smoke, hunger as well as fatigue etc. A human experiencing migraine is referred to as a migraineurs. It is important to note that migraineurs do not necessarily have to have all of the mentioned characteristics and factors. Distinguishing between milder migraine containing no aura from a headache that is moderate or severe can be quite challenging, however, there treatments are all similar. The international headache society have recognized and organized certain diagnostic criteria so that there is better and effective diagnosis of migraines. Some specialists have ruled out that organic disorders especially brain tumors are not associated with migraines.

In the diagnosis of migraine, patient history is usually the first step medical specialist conduct and it usually come out positive. However, there are other diagnostic approach can be used

such as physical examination, magnetic resonance imaging (MRI) or computerized axial tomography (CAT) to rule out that some of the symptoms are not organic pathology conditions. MRI are usually preferred imaging technique to investigate the head in the event of recent onset headaches which could also warrant the check of intraocular pressure. As mentioned earlier, the pain from migraine attacks is usually unilateral i.e. one sided, however, it can also be felt in the facial or cervical areas of the head which will occasionally observe a shift from area of occurrence to another area of the head. A typical victim of migraine will usually have one to five attacks of migraines in a month however, other victims experience the attack one to ten times in a month. Migraines are sometimes usually seasonal. Especially the frequency of migraines varies with seasons and even victims can identify the season of the year that they are more susceptible to migraine or have increased frequency. Patients usually experience bell shaped curve pain which is gradual ascent with a characteristic increase in level for some hours and then characteristics slow decline. The pain occasionally may reach peak as soon as the migraine onset. In another description, the pain and impact of migraines is throbbing, pounding, or pulsatile especially when the patients bend their head or simply the pain will be steady but with severe ache. Some patients may further experience pain impacts such as jabs of sharp pain which only for a short period of seconds. Nausea and vomiting are usually occasional with patients reporting that the aftermath of vomiting relieves the condition of migraines. When patients with migraines experience diarrhea (mild to moderate), it makes use of rectal suppositories very difficult

Among the characteristics of migraines that patients exhibit is that patients experience migraines that are accompanied by lightheadedness which may result to syncope. Syncope is referred to as the temporary loss of consciousness usually related to insufficient blood flow to the brain. In other words, patients fall faint regularly with migraine attacks. Majority of the patients become sensitive to light, sound as well as odors. Some less often characteristics of migraine attacks include pallor of face and flushing. Some patients might even experience some symptoms of fever like excessive low or high body temperatures. Some of these increase in temperature is usually at the site of occurrence of the migraine as well as regular cold feet and hands. Patients (migraineurs) often have experience of scalp tenderness which may last for some hours or some days during the migraine (prodrome) or even after the pain of the migraine attack is gone. The reason of tenderness of the scalp is contributed by two factors which are vascular and muscular factors. Disturbances usually autonomic are common and they may include autonomic disturbances like pupillary miosis or dilatation,

rhinorrhea, eye tearing and nasal stuffiness. Patients before or during or even after migraines may experience alteration of their moods such as anxiousness, tiredness, or depression etc. postdrome is the feeling patients feel after the migraine impact have seized. To summarize the characteristics of migraines we should consider some rare characteristics which may include euphoria, exhilaration, weight gain (usually less than six pounds) as a result of fluid retention in the body, polyuria. These are most of the general characteristics experienced by migraineurs as explained in this subsection.

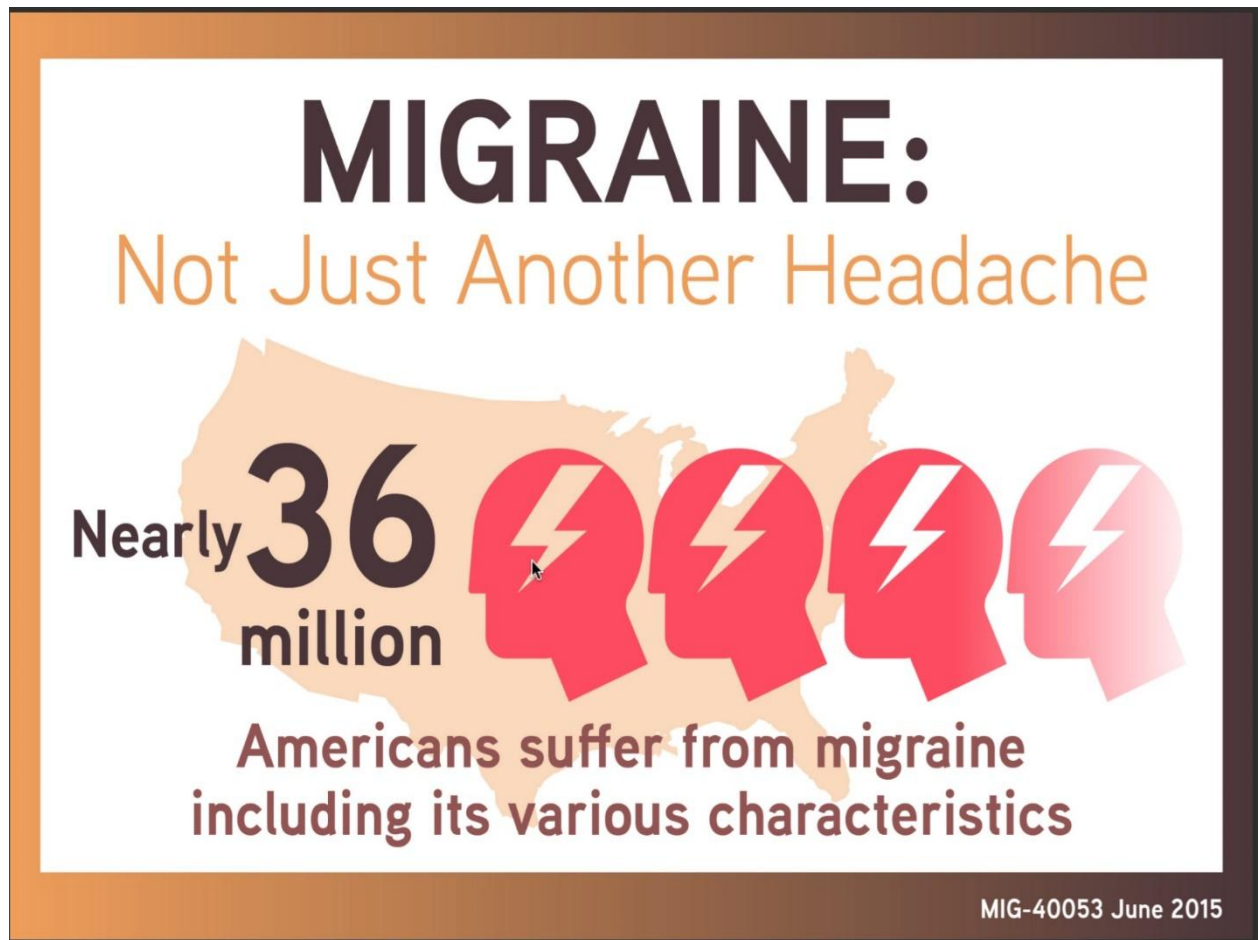


Figure 4: statistics of people with migraine in the United States

Retrieved from <https://www.mommyshangout.com/health-matters/a-migraine-is-more-than-just-a-headache/>

Overview of Migraine Medications

Since migraines is a serious health condition (neurological disease) and can potential threaten your life as well as your day to day activities, treatments of various kinds can be administered to patients. As can be seen in figure four where statistics showed that about 36 million Americans are attacked by migraines and women have more chances or experiencing the

neurological disease. It has been estimated by the American Migraine Foundation that in every four American households, at least a member is experiencing migraine attacks. As mentioned earlier, there is no clear cure of migraines, treatments are usually prescribed in order to ease the symptoms and characteristics of the attack. There are two approaches used in the treatment of the symptoms of migraines. Drugs and tablets prescribed or administered to patients are either meant to relieve the symptoms of the attack or prevent the occurrence of the attack. These are people who just depend on simple headache medications such as paracetamol, acetaminophen, anti-inflammatories (like naproxen, ibuprofen (Motrin), and a prescribed combination of barbiturate with narcotics), blood pressure medications, antidepressants, anti-seizure drugs, herbals and other antibiotics to relieve their pains. All these medications do not actually tackle the physiological processes that is the mastermind behind the occurrence of a migraine attack.

Before this current time, patients suffering from migraines have small choice of treatment because the attacks usually occur unilaterally (in parts of the head) which is as a result of dilation of blood vessels within the brain. But in modern times, modern drugs such as triptans have been clinically developed and made commercially available to relieve patient from this dilation of blood vessels in the brain in other words, it will cause the constriction of the blood vessels in the brain as well as breakdown the general chain of chemical events that are the reasons of the occurrence of the attacks of migraines. When migraine attack occurs to an individual more than once in a week or patient's migraines become unresponsive to abortive medications (more than half of the time), medical specialist will advise patients to move on to preventative therapy.

Different Type of Migraine Medications

There are two major categories to the medication of migraine attack, their impact or symptoms. The first approach is using drugs capable of aborting the progression or reoccurrence of migraines again while the other approach breakdown the general chain of chemical events that are the reasons of the occurrence of the attacks of migraines. Here is the list of Over-the-counter medications used impacted pain from migraines (NSAIDS and caffeine);

- Aspirin
- Naproxen (Naprosyn, Anaprox, Anaprox DS)
- Ibuprofen (Motrin)

- Acetaminophen (Tylenol)
- or the combination of all of these medicines such as barbiturate (also known as butalbital is a combination of acetaminophen, and caffeine with or without codeine (a narcotic)) and barbiturates

However, pain might get worst if patients continuously use these analgesics and NSAIDs medication daily. Also, these medications are only used for relieve and therefore do not resolve dilation of blood vessels in the brain. Moreover, ergotamines and triptans are used in blood vessel constriction.

Ergot alkaloids are potent drugs that constrict the blood vessel of the brain include medication such as ergotamine tartrate (Cafergot), dihydroergotamine mesylate, D.H.E. 45 Injection, as well as Migranal Nasal Spray. Some of the possible side effects of these ergot alkaloids medications include nausea. Some people who do not tolerate this side effect often prefer ergotamines in combination with other drugs to prevent nausea from occurring.

Triptans target serotonin receptors are considered more effective because they not only cause a constriction of the blood vessels in the brain, they also breakdown the general chain of chemical reactions that result in migraine. The following are notable triptans target serotonin receptors;

- Axert which stands for Almotriptan
- Relpax which stands for Eletriptan
- Frova which stands for Frovatriptan
- Amerge which stands for Naratriptan
- Maxalt, Maxalt-MLT which stands for Rizatriptan
- Imitrex, Zecuity which stands for Sumatriptan
- Zomig, Zomig-ZMT which stands for Zolmitriptan

Triptans were developed to be more migraine-specific, however there are specific triptans that are more strong in prevent migraines from occurring again. Despite these, all triptans are equally effective in providing patients with relief against migraines compared to other drugs (ergotamines). There are other drugs that have been developed to improve relief such as drugs containing vasoconstrictor isometheptene mucate, the sedative dichloralphenazone, as well as the analgesic acetaminophen (Midrin), Antihistamines- sedating (iphenhydramine) and non-sedating type (loratadine (Claritin)).

Side Effects of Migraines

Some of the general side effects experienced from medications of migraines are provided as bellow as follows;

- Head, jaw, chest, and arm discomfort, tightening, or tingling, Throat discomfort, Muscle cramps, Flushing, Gastrointestinal upset or bleeding
- Nausea, Vomiting, Rash, Liver damage
- Dizziness, Tingling, Flushing, Feelings of chest heaviness, burning, or tightness, Nausea, Headache
- Risk of heart attack or stroke, Stomach upset or bleeding, Nausea, Vomiting, Rash, Liver damage, Numbness of fingers and toes
- Stomach upset or bleeding, Rash, Swelling, and May raise risk of heart attack or stroke
- Heartburn, Anxiety, Insomnia, Allergic reaction, Liver damage, Blood in stool or vomit, Dizziness, Easy bruising, Dizziness, Tingling, Flushing, Feelings of chest heaviness, burning, or, tightness, Nausea

Causes and Triggers of Migraine

There is no specific known cause of migraines. Even researches have not reached a consensus regarded what actually causes migraines. However, it is widely thought to be as a result of abnormal neurological activities which temporarily affect the nerve signals, chemicals and blood vessels in the brain. These abnormal neurological activities could be a possible reason they happen but there is no clear cause of them. However, what researchers know is what triggers migraines.

Migraine Triggers

There are many possibly identified migraine triggers which can be classified in to hormonal, emotional, physical, dietary, environmental and medicinal factors that trigger migraines. Most an individual trigger to migraine is associate to one trigger factor but an individual can master them to sew which triggers are consistent and make them more susceptible.

1.2. Thesis Problem:

Migraines is a medical condition people across all spheres of life face at least every week if not every day. It may arise by various reasons such as stress, fatigue, hunger, and other medical conditions, etc. migraines can range in their severity and the location in which they occur. The migraine experience can also vary from one patient to another and maybe be due to mere stress or an indication or fever or other disturbing health conditions. There are

several treatment options for migraines. However, the most popular go-to options are treatment by drugs. There are several types of drugs and brands targeted in solving migraine problems some of which include paracetamol, nadolol, timolol, botulinum toxin type metoclopramide, domperdone, pizotifen, and sumatriptan, etc. it can be a difficult struggle choosing which drug among the vast drugs and brands that best suit a specific condition of migraine relating to patient or which one under general condition such as cost of drugs, drug to drug interaction, concentration, and drug efficient, etc. is best among the alternatives.

1.3. Aim of Study:

Analyse and classification the migraine drugs using fuzzy-PROMETHEE.

Determined and simulate the migraine drugs, which help us to take a good choice for treating the migraine disease.

For this reason, this thesis seeks to use fuzzy Prometheus, a multi-criteria decision-making technique to effectively compare 24 alternative migraine drugs that would assist medical professionals in administering effective migraine drugs in either in general situation or patient-specific situation.

1.4. Significance of the Study:

This study will enable the pharmacist to give the appropriate medication to the patient.

This study will enable the patient to obtain the appropriate medication in terms of efficiency and cost, making the best decision will be the result in less adverse effects on the patient.

This study will provide an explicit arrangement of the drugs used in the treatment of migraine based on efficiency and other parameters.

1.5. Limitations of the Study

All the data used for the research are secondary data, no original data was obtained in order to verify the consistency of the obtained data.

Different specialists have different opinions about the weight of each parameter.

No other decision-making software was readily available to make analysis in order to verify the results obtained from the VISUAL PROMETHEE software.

1.6. Overview of Thesis

Chapter 1 is an introduction of all thesis work include thesis problem, the aim of the thesis, significance, and limitation of the thesis, chapter 1 have the introductions of migraine disease, stages, different type, and cases of the migrant's disease. While chapter 2 discusses the medication that used to treat the migraine disease, dosage, side effect, interaction, and type of treatment.

Chapter 3 discuss the literature review of old study, while chapter 4 is the model or the methods that used to simulate the data and analyses the migraine drugs that used for treatment, Chapter 5 is the result of the simulated and analyses the data that we have it, while chapter 6 is the last chapter talks about conclusion and discussion.

CHAPTER 2

1.1. MIGRAINE DRUGS

In the United States about 6% of men and 17% of women are affected by migraine disorder (Weatherall M. W., 2015). Preventative and acute treatment are the two common divisions of migraine drugs (Weatherall M. W., 2015).

Acute migraine treatments.

Paracetamol 1 g

Aspirin 900–1200 mg

Ibuprofen 400–800 mg

Naproxen 250–500 mg

Triptans

Sumatriptan 50–100 mg orally, 10–20 mg nasal, 6 mg subcutaneously

Almotriptan 12.5 mg

Eletriptan 40–80 mg

Frovatriptan 2.5 mg

Naratriptan 2.5–5 mg

Rizatriptan 5–10 mg, s/l melt

Zolmitriptan 5–10 mg orally, s/l melt, 5 mg nasal

Combinations

Sumatriptan 50 mg and naproxen 250–500 mg

(all of the above are taken alone or with domperidone 10 mg orally, or an alternative antiemetic)

Single-pulse transcranial magnetic stimulation

Vagal nerve stimulation

Figure 5: treatment for acute migraine (Weatherall M.W., 2015)

Acute Treatment of Migraine

This treatment form is used as pain reliefs and for associated migraine headache symptoms. They are drugs taken when [auras or](#) the first symptoms of migraine are noticed and also to reduce the severity of a headache. These drugs when taken too often can lead to a [rebound headache](#), which then requires supplementary medication. Acute migraine drugs are not applicable for extended use of more than 9 times every month for persistent occurrence of the migraine instead preventive treatments would be prescribed. Examples include pain killers, triptans, ergotamines, anti-nausea drugs, opioids.

Painkillers: these can be provided over the counter in prescription strength. Common examples are diclofenac, aspirin, acetaminophen or paracetamol, ibuprofen and naproxen. These are non-steroidal and they are used relieve pain and inflammation. Side effects include stomach ulcers, stroke, kidney damage and heart attack.

Diclofenac

Diclofenac is a non-steroidal anti-inflammatory drug that reduce pain and inflammation causing substances in the body. This is used to treat mild symptoms of osteoarthritis or rheumatoid arthritis, mild-moderate pain of migraine headache attack. Diclofenac powder (Cambia) is used solely to treat a headache that has already begun. When used for a long time or in high doses, patients with heart disease have increased risk of a serious heart attack. The use of the drug is limited to patients who have under gone heart bypass surgery or have a history of allergic reactions to aspirin or NSAIDs (non-steroidal anti-inflammatory drugs).

Side Effects

Sneezing, hives, runny nose, wheezing or trouble with breathing happen as a result of allergic reactions to the drug. Indigestion, gas, diarrhea, constipation, nausea, chest pain spreading to the jaw or shoulder, rapid body numbness, slurred speech, increased blood pressure and shortness of breath are also some of the side effects experienced.
(<https://www.drugs.com/diclofenac.html>)

(<https://www.drugs.com/diclofenac.html>)

Aspirin

Molecular formula: $C_9H_8O_4$ Molar mass: 180.158g/mol IUPAC ID: 2-Acetoxybenzoic acid Melting point: 135 °C Boiling point: 140 °C Density: 1.4 g/cm³

Bayer is a German pharmaceutical company that maintains Aspirin as a trademark. Aspirin is known by its generic name as acetylsalicylic acid (ASA). Aspirin was one of the major non-steroidal anti-inflammatory drug (NSAID) to be discovered and have been used to treat blood thinning, as a pain reliever, for inflammation and fever. Patients that have high risk of stroke, heart attack and blood clots cannot use aspirin for long-term except administered in low doses. Rheumatic fever, pericarditis, and Kawasaki disease are specific inflammatory conditions which aspirin treats. It is usually given shortly after a heart attack to decrease the risk of death. ASA interacts with methotrexate, warfarin and other drugs.

Side effects: indigestion, deteriorating asthma symptoms, irritation of the stomach and vomiting, nausea, stomach bleeding due to inflammation, bruising, and in some cases hemorrhagic stroke.

(<https://www.medicalnewstoday.com/articles/161255.php>)

Paracetamol

Generic term: Acetaminophen

One of the first treatments recommended for pain is Paracetamol owing to the fact that it has rare side effects (<https://www.nhs.uk/conditions/paracetamol/>). Paracetamol is typically used to relieve mild or moderate pain, such as sprains or toothache, headaches and reduce flu fevers. It is available on prescription in the forms of capsules, tablets or caplets, injection into the vein (suppositories), liquid-usually for children and soluble tablets (dissolved in water). Paracetamol is combined with other ingredients in cold and flu drugs and painkiller combinations for example excedrin which is a combination of aspirin, caffeine and acetaminophen.

Side Effects

Although side effects are rare, when paracetamol is administered in the arm to patients with blood disorders; leukopenia and thrombocytopenia they can experience allergic reactions like

rash, fast heartbeat, low blood pressure and swelling. Overdose on Paracetamol can result in kidney and liver damage. (<https://www.nhs.uk/conditions/paracetamol/>).

Ibuprofen

This is another NSAID that works in a similar fashion as diclofenac by reducing pain causing substances in the body. The drug can also be used to treat pain resulting from arthritis, back pain, toothache, minor injury, menstrual cramps or inflammation as well as reduce fever and headaches. From the ages of at least 6 months old to adulthood the drug can be administered. Ibuprofen cannot be used by patients with recent heart bypass surgery and it could intensify the risk of a fatal heart attack due to long term use and patients with heart disease.

Side effects

Mild heartburn, upset stomach, constipation, nausea, vomiting, dizziness, headache, nervousness, a decreased appetite, rash with mild itching are common side effects of this drug. The drug should be stopped when there are changes in vision, kidney problems, difficulty in urinating due to pain, little or complete absence of the urine usually resulting in swollen ankles or feet. In more severe cases there are strokes or heart attacks, rapid numbness of the body, shortness of breath, chest pain and distorted speech.

(<https://www.drugs.com/ibuprofen.html>)

Naproxen

Generic term: naproxen (na-PROX-en).

Brand Names: Midol Extended Relief, EC-Naprosyn, Naprelan, Flanax Pain Reliever, Aleve and in combination with other medications: Aleve-D Sinus and Cold, Vimovo, Treximet and Aleve PM.

Naproxen as an NSAID works by reducing hormones or substances that cause inflammation and pain in the body. Naproxen is used to treat pain or inflammation caused by conditions such as arthritis, ankylosing spondylitis, tendinitis, bursitis, gout, or menstrual cramps. It can also be used to treat acute pain caused by other conditions not listed in this medication guide. The delayed-release or extended-release tablets are slower-acting forms of naproxen that are used only for treating chronic conditions such as arthritis or ankylosing spondylitis. These forms will not work fast enough to treat acute pain.

The usage of naproxen is limited and patients with a history of allergic reaction to aspirin or other NSAID (nonsteroidal anti-inflammatory drug) and also patients with heart disease cannot use it, Since it can increase risks of a fatal heart attacks or strokes during long term or high dose use.

Side Effects

Shortness of breath, indigestion, stomach pain, itching, nausea, dizziness or drowsiness, heartburn, swelling, rash, increased headache and bruising are common side effects of the drug. The drug is discontinued when heart attack signs, wheezing, and incoherent speech are noticed. (<https://www.drugs.com/naproxen.html>)

First line	Starting dose	Target dose
β blockers		
Propranolol	10 mg three times daily	40–80 mg three times daily
Metoprolol	25 mg twice daily	100 mg twice daily
Atenolol	25 mg once daily	100 mg once daily
Angiotensin blockers		
Candesartan	4 mg once daily	12–16 mg once daily
Tricyclics		
Amitriptiline	10 mg <i>nocte</i>	75–100 mg <i>nocte</i>
Nortriptiline	10 mg <i>nocte</i>	75–100 mg <i>nocte</i>
Dosulepin	25 mg <i>nocte</i>	75–100 mg <i>nocte</i>
Second line		
Anticonvulsants		
Topiramate	12.5 mg <i>nocte</i>	50–100 mg twice daily
Sodium valproate	200 mg <i>nocte</i>	400–800 mg twice daily
Flunarizine	5 mg once daily	5–10 mg once daily
Onabotulinum toxin A (Botox)	155 U (PREEMPT protocol)	
Supplements		
Riboflavin (vitamin B2)	400 mg daily	
Magnesium citrate (or taurate)	600 mg daily	

Figure 6: Preventative treatment for chronic migraine (Weatherall M.W., 2015)

Triptans

These are drugs that increase the serotonin levels of the brain, to reduce inflammation and constricting blood vessels hence effectively ending a migraine. There are available as pills and tablets that can be dissolved under the tongue, as injections and nasal sprays. These all work rapidly to reduce migraine. Examples of triptans are: eletriptan (Relpax), sumatriptan (Imitrex), naratriptan (Amerge), almotriptan (Axert), zolmitriptan (Zomig), frovatriptan (Frova), rizatriptan, (Maxalt, Maxalt-MLT), naproxen and sumatriptan (Treximet). There are three distinct pharmacological mechanism of action have been associated with the antimigraine effect of the triptans, they include (1) inhibiting both dural vasodilation and inflammation by stimulating the presynaptic 5-HT_{1D} receptors (2) directly inhibiting the trigeminal nuclei cell excitability through 5-HT_{1B/1D} receptor agonist present in the brainstem (3) meningeal, dural, cerebral or pial vessels vasoconstriction as a result of vascular 5-HT_{1B} receptor agonism. After 2-5 hours, absorption is rapid with peak plasma concentrations.

Almotriptan (Axert)

Generic-term: almotriptan (AL moe TRIP tan)

This is a headache medication used to constrict the blood vessels around the brain. Almotriptan like all NSAID reduces substances in the body that trigger migraine symptoms such as nausea headache pain, sensitivity to light and sound etc. This drug is suitable for adults and adolescents who are at least 12 years old. Almotriptan cannot be used to prevent a migraine from happening, common tension headache, and any headache that seems to be different from the usual migraine headaches or headaches that cause numbness of the body. It is used only as prescribed by a doctor to treat migraine headaches.

Side effects

Some of the side effects of the drug include; allergic reactions such as nausea, lightheadedness, sweating, tingling or numbness of a part of the body, appearance of a pale or blue-colored on the toes or fingers; blood circulation problems.

Naratriptan

Generic term: Naratriptan (nair-uh-TRIP-tan)

This is a triptan drug that is a sulfonamide selective for the 5-hydroxytryptamine₁ receptor subtype and typically used for the treatment of migraine headaches. Naratriptan has a role as a serotonergic agonist and a vasoconstrictor agent. It aids in relieving pain, headaches and the other symptoms of migraine. It has an Average weight of : 335.464 with a molecular formula of $C_{17}H_{25}N_3O_2S$. Common tension headaches, headaches different from the usual migraine headaches and headaches that come with loss of movement on one side of the body cannot be treated with this drug or administered to patients with high blood pressure that is uncontrolled, heart problems, certain heart rhythm disorders, severe kidney or liver disease, a stroke or heart attack history. Pregnant patients or those planning to become pregnant can take the drug only after duly informing their doctor since it is not been validated whether or not naratriptan passes into breast milk. It is recommended that the drug should not be taken after using another migraine headache medicine within 24 hours.

Side effects and drug interactions: The drug interactions can change how the drugs work or possibly increase the risks for severe side effects depending on the user. In cases where medications like ergotamine medication or any other "triptan" drug is used, the naratriptan dose is usually separated from the dose of these medications so as to lessen the risks of serious side effects e.g serotonin toxicity. Symptoms of overdose include fatigue, light-headedness, loss of coordination and tension in the neck.

Eletriptan

Another type of a triptan used to treat migraines is eletriptan. It affects a natural substance called serotonin to cause a narrowing of blood vessels in the brain. The effect is used to relieve pain affecting certain nerves in the brain. Eletriptan is prescribed for headache, pain, and other migraine symptoms. Early treatment enables patients return to their normal routine and also decrease the necessity to use any other pain medications. It is an acute migraine treatment and does not prevent future migraines or reduce the frequency of migraine attacks.

Side effects: Very serious allergic reactions are rare, difficulty and shortness of breath, seizures, serious stomach pain and bloody diarrhea, severe chest pain, irregular heartbeats,

numbness, weakness of the muscles, burning pain, hip pain, symptoms of heart attack, sweating. The increased levels of serotonin in the body can cause hallucinations, blurred vision, increased blood pressure, fainting, fever, overactive reflexes, agitation, fast heart rate, loss of coordination, increased headache. Pregnant patients or those planning to become pregnant can take the drug only after duly informing their doctor since it is not been validated whether or not naratriptan passes into breast milk. It is recommended that the drug should not be taken after using another migraine headache medicine within 24 hours.

Rizatriptan

This drug acts like other triptans by reducing the effect of substances that cause the narrowing of blood vessels in the brain hence it is used to treat headaches. A popular brand name for this is Maxalt. Rizatriptan an acute treatment for migraine so it is not used to prevent the frequency of occurrence of a migraine headache.

Side effects: numbness, difficulty and shortness of breath, seizures, serious stomach pain and bloody diarrhea, severe chest pain, irregular heartbeats, weakness of the muscles, burning pain, hip pain, symptoms of heart attack, sweating. The increased levels of serotonin in the body can cause hallucinations, blurred vision, increased blood pressure, fainting, fever, overactive reflexes, agitation, fast heart rate, loss of coordination

Frovatriptan

Frovatriptan is a triptan that also reduces substances in the body that can generate migraine pain symptoms like, headaches, nausea, sensitivity to light and sound. It has a unique long-half life, which is five times that of any other triptan. For this reason it provides an opportunity for its use in mini-prophylaxis such as in menstrual-related migraine and other situations, as well as use in long-lasting or recurrent migraine. Frovatriptan has a high affinity for 5-HT_{1B} and 5-HT_{1D} receptors and a moderate affinity for the 5-HT_{1A} and 5-HT_{1F} receptors subtypes. Frovatriptan has been shown to be one of the most potent 5-HT_{1B} agonists (Brown et al and Stewart et al, 1998). Another difference from frovatriptan has is that it portrays a moderate affinity for the 5-HT₇ receptors (Brown et al and Stewart et al, 1998). As with other triptans accurate diagnosis of migraine must be made before its use. Early use of the drug is always advised moderate or severity of a migraine attack starts (Cady et al, 2004). The medication is recommended to be used continuously after 2 hours if needed and should not be used more than 2 days in a week on a consistent dose basis. Rescue

medication for pain and nausea and vomiting should be prescribed to obviate the need for emergency room visits. In Kelman L. (2008), it was suggested that if frovatriptan was not successful for acute treatments after a two headache trial, anti-inflammatory should be added to increase potency otherwise, other alternative triptans should be considered.

Frovatriptan can only treat a headache that has already begun.

Side effects:

A doctor has to be consulted before use by pregnant patients, blood circulation problems, heart disease and uncontrolled high blood pressure, sleep disorder migraineurs and Wolff-Parkinson-White syndrome. Some common side effects include; difficulty and shortness of breath, seizures, serious stomach pain and bloody diarrhea, severe chest pain, irregular heartbeats, numbness, weakness of the muscles, burning pain, hip pain, symptoms of heart attack, sweating. The increased levels of serotonin in the body can cause hallucinations, blurred vision, increased blood pressure, fainting, fever, overactive reflexes, agitation, fast heart rate, loss of coordination, increased headache.

Sumatriptan:

Sumatriptan is a drug belonging to the triptan family and used in the abortive medication of migraine attacks. At serotonin 5-HT₁-like receptors and 5-HT_{1B/1D} subtypes sumatriptan is a selective agonist, hence it is effective in the treatment of acute migraine attacks. In studies done the injectable form has also revealed efficacy in the treatment of cluster headache cases (Perry & Markham, 1998).

Side effect: malaise, vomiting, fatigue and nausea are the most common adverse events with oral sumatriptan. Reactions at injection site occur in 10 to 40% of patients receiving the drug subcutaneously, such as a bitter taste at the back of the mouth occurs frequently after intranasal administration. Severe adverse events were reported in about 0.14% of patients with migraine treated with sumatriptan (Perry & Markham, 1998). Patients with a history of cardiovascular disease cannot use sumatriptan except specifically given by a doctor. For first- or second-line treatment option for patients with moderate or severe migraine the drug is recommended (Perry & Markham, 1998).

Zolmitriptan:

Like other triptans, preclinical studies have presented that zolmitriptan is also selective at serotonin 5-HT (1B/1D) receptor agonist (triptan). During placebo-controlled, randomized, and double-blind trials in patients with migraine, zolmitriptan was shown to have good efficacy. Zolmitriptan tablet taken orally has an advantage since it may be taken immediately, devoid of the need for additional fluids, once a migraine headache occurs. The improved efficacy from the convenience of the disintegrating tablet, the nasal spray form are effective ways of taking in the treatment of migraine or auras. This drug is suitable first-line therapy and acceptable by patients for the treatment of migraine (Bruce Charlesworth and Andrew J Dowson 2002)

Side effects: this drug has side effects that are similar to the drugs in the triptan class of drug. It cannot be used for patients that have uncontrollable high blood pressure, problems associated with the heart and blood circulation problems.

Ergotamine: : has a molecular weight of 581.673 g/mol. Powder or liquid forms available as drugs. It is used in obstetrics and in the treatment of migraine headaches. (EPA, 1998). Molecular formula of $C_{33}H_{35}N_5O_5$. This drug is a naturally occurring ergot alkaloid with analgesic and vasoconstrictor properties. Ergotamine binds and activates serotonin (5-HT) 1D receptors selectively causing vasoconstriction and reduced blood flow around the cerebral arteries to relieve vascular headaches. To stimulate vascular smooth muscle ergotamine binds to an alpha-adrenergic receptors also to cause vasoconstriction in arteries and veins in order to relief of headaches.

Side Effects

This have severe side effects such as; birth defects, heart problems and they can be toxic when used in high doses. Pregnant, breastfeeding and heart disease patients are advised not to use ergotamine. This drug can also interact negatively with other drugs such as antibiotic and antifungal drugs.

Calcium channel blockers

Calcitonin gene related peptide antagonist CGRP (gepants)

Gepants, monoclonal antibodies, or calcitonin gene related peptide antagonist, CGRP blockers are receptor antagonists with an interesting group of molecules used as possible new treatments for migraine. A vasoconstrictive effect is not observed from these group of molecules and thus are not conventional treatments (Tso and Goads by 2014). They instead target specific migraine mechanisms and they represent the most productive class of migraine treatment drugs since they have multiple agents that target CGRP or its receptor, for these they are still under development as both preventive and acute migraine treatment.

Beta-blockers

It is a preventative treatment for migraine. Atenolol, timolol, Metoprolol, Nadolol, Propranolol are beta blockers. They are prescribed to patients with high blood pressure to reduce the effects of stress hormones.

Side effects: common side effects are nausea, dizziness, fatigue, insomnia and depression.

Propranolol

This belongs to a class of beta blockers. It can be found under the brand name of Inderal, InnoPran XL and Hemangeol. It can be used to control heart rhythm in atrial fibrillation, support heart function after a heart attack and prevent migraines. Propranolol works by acting on nerve impulses in specific areas of the body. This drug is mostly taken orally once a day with effects that lasts for up to 24 hours.

Side effect

Common side effects are; dry eyes, fatigue, slower heart rate, diarrhea, wheezing, drowsiness and sometimes hair loss.

Atenolol or Tenormin

Generic term: atenolol

This belongs to a class of drugs called the beta-blockers and Beta-1 Selective. The mechanism of action is to block natural chemicals action in the body, chemicals like epinephrine present in the blood vessels and heart. The drug lowers the blood pressure, heart rate and strain on the heart. Like other beta-blockers atenolol is a first-line choice for episodic migraine prophylaxis. Edvardsson B. (2013) showed that Clinical findings support the effectiveness of atenolol in doses of up to 50-200 mg/day. This drug is used in the prophylaxis of chronic migraine during a 3-month open-label study. Apart from preventing migraine headaches, Atenolol may also be used to treat heart failure, alcohol withdrawal symptoms and irregular heartbeat and with other medication to treat hypertension

Side Effects

Several effects of this drug are; dry eyes, visual disturbances, hypotension, tiredness, hallucination, reduced heart rate, dizziness and drowsiness, visual disturbances and reduced performance in neuropsychometric test and short term memory, impotence, purple colored spots on the skin, rashes, atrioventricular block, pain in the legs, thrombocytopenia, elevated serum hepatic enzymes and bilirubin, antinuclear anti bodies (ANA), sick sinus syndrome, disorientation, serious congestive heart failure (CHF), Raynaud phenomenon, impotency, lupus syndrome, Peyronie's disease and psychoses.

Metoprolol also known as Toprol XL

This beta blocker works by relaxing blood vessels in order to slow the heart rate. The effects are lowering blood pressure and improving blood flow. Brand names that exists for this is Toprol XL which is prescribed for the treatment of heart failure. It can also be used to treat migraine and other heart conditions. For patients with asthma, hyperthyroidism, congestive heart failure, diabetes and certain allergies the reactions can become worse with continuous use of metoprolol.

Side effects

Side effects are similar to beta blocker drugs. Dizziness, nausea, dry mouth and so on.

Nadolol this is a nonselective beta-adrenergic receptor blocking agent with brand name Corgard. It is used by angina patients, to slow down the heart rate. It is also prescribed to patients with chronic migraine headaches, tachycardia, postural orthostatic tachycardia syndrome, and high blood pressure. This can be administered in oral form as tablets.

Side effects

Cold hands and feet due to the reduction of blood flow in them. Drowsiness, weakness, dizziness and cough may occur. Overdose of the drugs can cause serious symptoms such as passing out as a result of troubled breathing, slow heartbeat and severe dizziness.

Timolol: Blocadren is the brand name for this drugs. Just like propranolol timolol has consistently shown efficacy in prevention of episodic migraine. It is also a beta-blocker type of drug.

Side effects: include, fatigue, constipation, nausea, vomiting, and diarrhea.

Pizotifen: Pizotifen is a derivative of benzocycloheptathiophene that affects some biogenic amines due to its strong antagonistic action. It does not treat acute migraine attacks but can be used in the prophylactic treatment of severe and recurring vascular headaches.

Botulinum toxin type A

Botulinum toxin type A is a Botox (Botulinum toxin type A) injections FDA approved which can be injected in neck muscles and on the forehead as a chronic migraine treatment. It is expensive and can be repeated every three months.

Side effects

Stiffness and neck pain, partial weakness of the muscles of the neck. Other side effects are flu like symptoms like fever and temporary drooping of the eyelid.

Metoclopramide This is effective in the treatment of nausea and pain from migraine headache, which has no dependence on the concomitant administration of another agent (GL, J, & DeHart DA, 1993). In (Najjar, Hall, & Estupinan, 2017) metoclopramide was investigated to be a more effective alternative to opioids for the treatment therapy for acute migraine. Metoclopramide is a mild analgesic which can be administered in oral form.

Side effects: regardless of the efficacy of metoclopramide side effects are serious and irreversible. The effects consist of dyskinesia (involuntary movement of the face and tongue)

Domperidone: this is a dopamine receptor blocker used in the treatment of aura onset as a preventative step. It is also a prokinetic agent prescribed during the prodromal phase of migraine. It is available in oral formula and it shortens the duration of migraine attacks without causing adverse effects

Side effects: Dry mouth, dizziness, Headaches, hot flashes, stomach cramps, discharge from nipple in men and women are common side effects of domperidone.

Phenothiazine is a dopamine agonists that is neuroleptic. It is combined with triptans for use in the treatment of acute migraine.

Side effects: low blood pressure, headaches, blurred vision, muscle spasm and drowsiness are common side effects.

Antihistamine: migraine symptoms can be treated with these by counteracting the effects of histamine (substance present in the body that dilates the blood vessels to cause an inflammatory reaction).

Side Effect

Low blood pressure, dizziness and drowsiness, blurred vision, increase in the thickness of lungs secretion, serious allergic reaction and seizures are some of the common side effects of this drug.

Table 1: Medicines that can be used for the treatment of migraine with typical dosing regimen (Ryan, S. 2007).

Preventative drugs	Suggested dosing regime	Common or key side effects and contraindications	Comments	Rationale
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Pizotifen	5–10 years Start with 250 mg at night and increase up to 1 mg (occasionally 1.5 mg) at night 10–12 years Start with 0.5 mg at night then as above 12–18 years Start with 1.5 mg at night then increase up to 3.0 mg at night	Drowsiness, dizziness which often settle Weight gain and increased appetite, occasional behavioural disturbance	Usually well tolerated as single night time dose; try and avoid daytime use to reduce drowsiness Weight gain very common due to increased appetite Not very popular with teenage girls who must be made aware of this Use for 3–6 months in first instance and then review as migraine activity frequently dissipates	BNF-C +++ Licensed +++ Cochrane Children +/- Custom and practice +++
Propranolol	2–12 years 10 to 20 mg twice a day 12–18 years 20 to 40 mg twice day	Contra-indicated in asthma Depression, postural hypotension, cold peripheries, insomnia	Athletes who rely on adrenaline kick may not be too keen on it Use for 3–6 months in first instance and then review as migraine activity frequently dissipates	BNF-C +++ Adult BNF +++ Off-label + Cochrane + Custom and practice ++
Topiramate	Over 16 years 25 mg at night increasing to 50 mg twice daily as required	Reduced appetite, weight loss, gastrointestinal, headache, impaired memory and concentration		BNF-C 2 Adult BNF +++ Licensed 16 years Controlled trials +
Amitriptyline	Teenagers 25 mg at night increasing to 75 mg as necessary	Very toxic in overdose Dry mouth, sedation, dizziness, behaviour problems	Not recommended for depression treatment in under 16s May be useful in chronic fatigue complex with headache Is still licensed for nocturnal enuresis Initial side effects very common usually subside; ensure patient aware of this as improves concordance with therapy	Adult BNF++ Off-label Cochrane – Controlled trials -

Sodium valproate	About half the dose indicated for epilepsy and increase as necessary up to maximum epilepsy dose	Weight gain, dry skin, alopecia, behavioural disturbance, liver function test transaminase elevation; very rarely hepatitis and pancreatitis	Possible weight gain is a significant concern for children and families; check weight status Concerns over teratogenicity	Adult BNF++ Off-label Cochrane adults ++ Controlled trials 2
Gabapentin	12–18 years Start with Gabapentin 100 mg three times daily and increase up to 300 mg three times daily	Dizziness, drowsiness	Usually well tolerated Useful for mixed headache with chronic daily headache component	Cochrane adults ++
Acute treatment Paracetamol	1–12 years 20 mg/kg every 6 h (maximum dose 90 mg/kg in 24 h) 12–18 years 0.5–1 g every 6 h	Rare	Risk is with potential overdose a liver damage Use soluble or liquid form. Works for some tension headaches Risk of analgesic headache with frequent use	BNF-C +++ Cochrane children+ Licensed
Ibuprofen	2–18 years 10 mg/kg/dose each 8 h	Rarely gastrointestinal upset Caution with previous hypersensitivity to NSAID	Evidence of superiority to paracetamol in migraine weak Use soluble, liquid or orodispersible form if possible Works for some tension headaches Risk of analgesic headache with frequent use	BNF-C +++ Cochrane children + Licensed
Sumatriptan (nasal)	>12 years 10 mg at onset and repeat once only at 2 h if needed	Unpleasant taste and smell, heavy, tight or unusual feeling anywhere in body but often neck	Use as soon as possible in attack Does not work for tension headache types	BNF-C +++ Cochrane children + Licensed
Codeine	Up to 12 years 0.5–1 mg/kg every 6 h Over 12 years 30–60 mg every 6 h	Sedation, constipation Respiratory depression in overdosage	Use in conjunction with paracetamol for synergistic effect (eg Migraleve)	BNF-C ++ Licensed Cochrane children –

Meto- clopramide	Complex dosing schedule—see BNF-C (around 100 mg/kg/dose every 8 h up to 9 years and 5 mg per dose from 9 years)	Dystonic reaction, drowsiness	Used in combination with paracetamol or other analgesic eg Paramax	BNF-C ++ Licensed Cochrane 2
Domperidone	.2 years & weight,35 kg 250–500 mg/kg 8 hourly Weight .35 kg 10–20 mg every 8 h	Rare	Use with analgesic	BNF-C + Licensed

Level of Care	Acute treatment	Preventative treatment
Level 1. Self care	Paracetamol, Ibuprofen	Avoidance of triggers
Level 2. Primary care—simple non-prescription analgesics ineffective	Codeine Domperidone Metoclopramide	Pizotifen Propranolol
Level 3. Secondary care—licensed treatments ineffective or require specialist initiation of therapy	Nasal sumatriptan High flow oxygen	Topiramate, amitriptyline, valproate, gabapentin
Level 4. Tertiary care—very resistant and unusual headache disorders		Verapamil Indomethacin

Figure 7: Hierarchy of migraine treatment (Ryan, S.2007)

Flurbiprofen

This is an NSAID that works by reducing pain from inflammation causing hormones in the body such as pain from rheumatoid arthritis or osteoarthritis. Flurbiprofen can intensify the risks of a severe stroke or heart attack, during long term or high dose use.

Side effects may include: confusion and dizziness, headache indigestion, stomach pain, nausea, vomiting, increased sweating, tremors and nervousness, constipation, diarrhea, drowsiness, rash and itching.

(<https://www.drugs.com/mtm/flurbiprofen.html>)

CHAPTER 3

LITERATURE REVIEW

Various fields such as chemistry, engineering, medicine and even social studies have very recently started to apply Multi-criteria decision-making (MCDM) techniques to improve the quality of life. Many researchers have carried out studies on it using several MCDM techniques for example; Simple Multi-Attribute Rating Technique (SMART), PROMETHEE (Outranking) , Analytic hierarchy process (AHP), ELECTRE (Outranking) and other techniques are available (Weistroffer, Smith & Narula, n.d.).

In (Brans, Vincke & Mareschal, 1986) PROMETHEE ranking is said to be one of the most common of these decision-making tools, which was developed as an outranking method to obtain outranking of a defined combinations of real-world actions which were either a partial or complete.

Using experimental data available at a public hospital in Brazil a research was conducted to analyze and support the process of decision-making and resource management within the emergency department Amaral and Costa (2014) applied PROMETHEE II. A few months after its implementation the solution of the analysis obtained from their research showed that the waiting time during overcrowding periods in the waiting room was reduced by about 70%. It was concluded that PROMETHEE enables a decision maker to select the best options to solve problems due to overcrowding in the emergency departments of hospitals and that this method can be extended to other departments in the hospital.

Different multi-criteria decision methods were used by Silas and Rajsingh (2016) to analyze healthcare services application. ELECTRE, PROMETHEE and AHP were MCDM methods selected for the analysis. The criteria also selected were chosen with varying degrees of preferences, the time taken to select the health care services, the average overhead incurred in selection of the health care services, the patient satisfaction based on the overall performance and degree of human intervention. Results from their analysis indicated that PROMETHEE is a suitable MCDM tool for application in healthcare service analysis with 95% of users preferring PROMETHEE algorithm for the selection of a healthcare service.

Drawing from their previous study using fuzzy PROMETHEE Ozsahin et al. (2017), evaluated cancer treatment alternatives by comparing different existing cancer treatment techniques; chemotherapy, radiation therapy, hadron therapy, immune-therapy, hormone

therapy and surgery. Using similar methods from the previous study the primary factors that could affect the outcome of a chosen treatment technique they selected side effects, cost of treatment, survival rate and treatment duration. The hadron therapy bested all the alternatives with the highest survival percentage, shortest time for the treatment and combined net-flow value of 0.4931 and the most suitable treatment technique for a cancer patient.

Ozsahin et al. (2017) evaluated and compared the most common imaging devices available in nuclear medicine, using techniques for multi-criteria decision-making. These imaging devices assessed were Single Positron Emission Computed Tomography (SPECT), Positron Emission Tomography (PET), PET/MRI, SPECT/CT and PET/CT. The parameters for the comparison were cost of treatment, average radiation dose, average scan time, energy resolution, sensitivity and specificity of the device and spatial resolution. In this study Yager Index was applied to determine the magnitude of the triangular fuzzy numbers. Visual PROMETHEE Decision Lab Program was used and the preference function was set to Gaussian preference function in order to arrive at their results. PET was ranked best with a net-flow of 0.0005 is a more beneficial and advisable imaging device based on the parameters used.

In another study by Ozsahin et al. (2018) the most commonly employed techniques for image construction algorithms used in nuclear medicine were compared, by using the fuzzy PROMETHEE method. The comparison included Filtered Back Propagation (FBP), Origin Ensemble (OE), List Mode-OSEM (LM-OSEM) and Ordered Subset Expectation Maximization (OSEM) which are the most commonly used image construction algorithms to produce images of desirable features which are of higher quality in nuclear imaging. Variance, Mean Square Error (MSE), Uniformity, Run Time, Resolution Compensation (RC), Bias and Modulation Transfer Function (MTF) were selected as the parameters for comparison in the study. The results of their study obtained showed that, FBP is a superior algorithm for higher quality images, with a net-flow of 0.0031.

Ozsahin et al. (2018) used Fuzzy Preference Ranking Method for Enrichment Evaluations to evaluate x-ray based medical imaging devices. They applied fuzzy PROMETHEE to evaluate the image quality parameters of some x-ray based devices to determine the efficiency, potentiality and disadvantages of each device. The parameters utilized in their studies to make these analysis were specificity, sensitivity, the treatment cost, radiation dose, as well as the cost of the machine. The parameters were chosen and analyzed based on the effects they have on the patient as well as the hospital. The devices that were put into consideration for

these analyses are conventional x-ray machine, angiography, Computed Tomography (CT), fluoroscopy and mammography. Yager index was used to view the magnitude of the parameters for each of the alternatives. Their results rank the conventional x-ray machine as a suitable imaging device when the cost of machine is not put into consideration with a net flow of 0.0017. While mammography outranked the other medical imaging devices when the cost of machine is put into consideration with a net flow of 0.0015.

Ozsahin and Ozsahin (2018) made a fuzzy PROMETHEE approach for breast cancer treatment techniques to analyze and rank the most suitable treatment technique for patients diagnosed with breast cancer. In their research, surgery, radiotherapy, chemotherapy and hormone therapy treatment techniques for breast cancer, using parameters such as overall survival rate of each technique, side effects, cost of treatment and treatment time were chosen. The conclusion of their studies ranked surgery as the most suitable treatment technique for patients with breast cancer, amounting a net flow of 0.5156, based on the parameters that they used.

CHAPTER 4

METHODOLOGY

4.1. Fuzzy Logic

Decision making requires obtaining data that can correctly represent real models in different fields such as engineering and in medicine. However these data are often vague and imprecise. A form of algebra centered on the idea that all values can either be true or false (0 or 1) called Boolean logic can be applied to creating concepts that approach machine language and it supports logical outcomes. This method allows (1) or false (0), no room for in-betweens or uncertainties is allowed. Another logic introduced was fuzzy logic which catered for the uncertainty in data available to a certain degree. In Boolean logic a cooling system can be operated as either high or low, in events when an operator may want levels of control of the cooling system, fuzzy logic can be applied. Hence alternative levels of cooling can be created to depict very high levels, high level, moderate level, low level and very low level. These alternatives presume uncertainty in real working conditions unlike the Boolean system.

Bayesian control, classical theory predictable logic, probability theory, and so many such systems in terms of computing with words makes Fuzzy logic more preferred. A system of, meaning words are used to represent numbers in computing and reasoning when using Fuzzy logic (Zadeh, 1996).

4.2. Multi-criteria Decision-Making

Multiple-criteria decision analysis (MCDA) sometimes referred to as Multi-criteria decision-making (MCDM) is an area of research that provides solution through analysis of various available choices and objectives in different facets of research and everyday life. (Marandi et al., 2015) stated that MCDM is one of the mostly applied decision-making tool in various fields.

The criteria involved in a parameter that makes the parameter a favorable or unfavorable choice can be analyzed using MCDM for a particular application and it attempts to compare these parameter based on the selected criteria, against every other available option in an attempt to assist a decision maker to select an option with less than or no compromise but with maximum advantages. These selected criteria are evaluated according to expert knowledge and can be either qualitative or quantitative parameters or evaluated together.

MCDM can be discussed in two categories based on the method used to determine the weight of each alternative (Majumder, 2015):

- i. Compensatory decision-making: the criteria of the parameters is evaluated to include the weak points and the strong points of the parameters and to allow the strong points of each parameter to make up for the weak points, thus all the criteria of the parameters are considered. An example of compensatory decision-making tool is the Analytical Hierarchy Process (AHP) a technique mostly applied in the analysis of complex environment. It is used in the comparison of parameters that are difficult to quantify.
- ii. Outranking decision-making: compares the criteria of the parameters in sets in order to determine which parameter would rank higher than the others accordingly (Yang, Wang & Wang, 2012). ELECTRE (Elimination and Choice Expressing Reality) is an example of an outranking method for decision-making that is used to choose, rank and sort out available alternatives to solve a problem.

4.3. A Preference Ranking Organization Method for Enrichment Evaluations (PROMETHEE).

This is a decision-making tool applied when there are multiple criteria that can be used to analyst and rank available alternatives. PROMETHEE which ranks based on the criteria of each alternative. This tool compares the available options or choices based on the selected criteria by the user.

The suitability of use of PROMETHEE in its application to multiple decision modelling falls under several reasons such as;

- The use of fuzzy numbers for fuzzy relations, vagueness and uncertainties.
- The MCDA provides the user enables easy manipulations and maximum control over the weights of the criteria.
- PROMETHEE can be used to handle qualitative and quantitative criteria simultaneously.

The elements required for using PROMETHEE are;

- i. the weights of the selected criteria are derived from the decision maker's information
- ii. A preference function is to be applied while comparing the alternatives' contribution with regards to each criterion (Macharis, Springael, De Brucker & Verbeke, 2004). In PROMETHEE preference functions (P_j) are widely

available for the definition of different criteria. Preference functions define the difference between two or more evaluated alternatives (a_i and a_j) in relation to a specific criterion and a preference degree ranging between 0 and 1. For practical purposes the preference functions can be used at the discretion of the decision maker some of which are; Gaussian function, V-shape function, level function, u-shape function, linear function and usual function. In figure 8, J. P. Brans et al. describes a quick summary of the preference functions showing the preference functions applied, their ranking and how to make a decision on which function best fits a scenario (Brans, Vincke & Mareschal, 1986). Generally, type III (v- shape) and type V (linear) preference functions are mostly used for data with quantitative measures, while type I (usual shape) and type IV (level) preference functions are mostly used for qualitative data.

The significance of the parameters to be defined are as follows;

- -where q shows a threshold of indifference.
- -and p is a threshold that indicates strict preference.
- -while σ is an intermediate point between q and p .

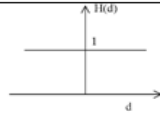
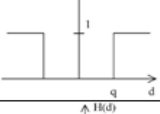
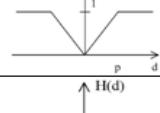
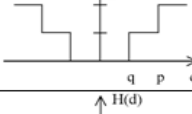
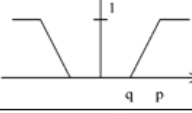
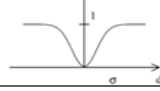
Type of generalized criteria	Analytical definition	Shape	Parameters to define
Type I. Usual criterion	$H(d) = \begin{cases} 0, & d = 0; \\ 1, & d > 0. \end{cases}$		—
Type II. Quasi-criterion	$H(d) = \begin{cases} 0, & d \leq q; \\ 1, & \text{otherwise.} \end{cases}$		q
Type III. Criterion with linear preference	$H(d) = \begin{cases} \frac{ d }{p}, & d \leq p; \\ 1, & d > 0. \end{cases}$		p
Type IV. Level-criterion	$H(d) = \begin{cases} 1, & d \leq q; \\ 1/2, & q < d \leq p; \\ 0, & \text{otherwise.} \end{cases}$		q, p
Type V. Criterion with linear preference and indifference area	$H(d) = \begin{cases} 1, & d \leq q; \\ \frac{ d - q}{p - q}, & q < d \leq p; \\ 0, & \text{otherwise.} \end{cases}$		q, p
Type VI. Gaussian criterion	$H(d) = 1 - \exp\left\{-\frac{d^2}{2\sigma^2}\right\}$		σ

Figure 8: Generalized preference functions for PROMTHEE

4.3.1. The Steps of the PROMETHEE Method

(Brans, Vincke & Mareschal, 1986), were the creators of the technique and also created the complete steps of the PROMETHEE method, alteration to this method has not been made in any way for this research.

1. First a specific preference function $p_j(d)$ for each criterion j is defined.
2. Determination of the weight of each criterion $w_t = (w_1, w_2, w_k)$. Normalization of weights or equality of weights can be decided at the discretion of the decision maker based on the application.

3. Determination of the outranking relation π for every alternative $a_t, a_{t'} \in A$,

$$\pi(a_t, a_{t'}) = \sum_{k=1}^K w_k \cdot [p_k(f_k(a_t) - f_k(a_{t'}))], \quad AXA \rightarrow [0,1]$$

4. Determination of the positive and negative outranking flows;

- Positive outranking flow for a_t : $\Phi^+(a_t) = \frac{1}{n-1} \sum_{\substack{t'=1 \\ t' \neq t}}^n \pi(a_t, a_{t'})$
- Negative outranking flow for a_t : $\Phi^-(a_t) = \frac{1}{n-1} \sum_{\substack{t'=1 \\ t' \neq t}}^n \pi(a_{t'}, a_t)$

n refers to the number of alternatives, and each alternative is compared to an $n-1$ number of alternatives.

A positive outranking flow is an expression of how one of the alternatives produces the best results better than the other alternatives in terms of the selected criteria. The higher the positive outranking value of a particular alternative is, the better the alternative.

And a negative outranking flow is an expression of how a particular alternative is bested by other alternatives. The lower the negative outranking value is, the better the alternative.

5. Define the partial preorder on the alternatives of A . PROMETHEE I provides that alternative a_t is preferable to alternative $a_{t'}$ ($a_t P a_{t'}$) if it satisfies the one of the following conditions:

$(a_t P a_{t'})$ if;

$$\begin{cases} \Phi^+(a_t) > \Phi^+(a_{t'}) \text{ and } \Phi^-(a_t) < \Phi^-(a_{t'}) \\ \Phi^+(a_t) > \Phi^+(a_{t'}) \text{ and } \Phi^-(a_t) = \Phi^-(a_{t'}) \\ \Phi^+(a_t) = \Phi^+(a_{t'}) \text{ and } \Phi^-(a_t) < \Phi^-(a_{t'}) \end{cases}$$

If there are two alternatives $(a_t \text{ and } a_{t'})$, with similar or equal leaving and entering flows, a_t is indifferent to $a_{t'}$ ($a_t I a_{t'}$):

$$(a_t I a_{t'}) \text{ if: } \Phi^+(a_t) = \Phi^+(a_{t'}) \text{ and } \Phi^-(a_t) = \Phi^-(a_{t'}).$$

a_t is incomparable to $a_{t'}$ ($a_t R a_{t'}$) if;

$$\begin{cases} \Phi^+(a_t) > \Phi^+(a_{t'}) \text{ and } \Phi^-(a_t) > \Phi^-(a_{t'}) \\ \Phi^+(a_t) < \Phi^+(a_{t'}) \text{ and } \Phi^-(a_t) < \Phi^-(a_{t'}) \end{cases}$$

6. Determination of the net outranking flow for each alternative

$$\Phi^{net}(a_t) = \Phi^+(a_t) - \Phi^-(a_t)$$

Using PROMETHEE II, a complete preorder would be produced by the net flow and defined by:

a_t is preferable to $a_{t'}$ ($a_t P a_{t'}$) if $\Phi^{net}(a_t) > \Phi^{net}(a_{t'})$

a is indifferent to $a_{t'}$ ($a_t I a_{t'}$) if $\Phi^{net}(a_t) = \Phi^{net}(a_{t'})$.

In other words, the most suitable alternative would be the one having a higher $\Phi^{net}(a_t)$ value.

4.4. Application of PROMETHEE to the Project

The weight of each criterion is determined through defuse fiction of the triangular fuzzy numbers by applying the Yager index. The Yager index puts into consideration all the points and is not hugely affected by extreme values or weights hence it is preferred over other methods.

CHAPTER 5

RESULT AND FINDINGS

From the conducted analysis, our result indicated that the migraine drug, pizotifen which showed excellent performance in terms of dose frequency, cost, half-life, drug to drug interaction, absorption, and number of tablet . However, pizotifen was found to have poor performance in to terms of efficacy and side effect. The positive outranking flow of pizotifen is 0,5566 while the negative outranking flow is 0,0785. On the other hand, the migraine drug, sumatriptan was ranked the lowest due to it poor performance in efficacy and side effect, drug to drug interaction, half-life, dose frequency, absorption, and cost. It was found to perform well only in number of tablet and side effect with a positive and negative outranking flow of 0, 1295 and 0, 4930 respectively. A complete ranking of the migraine drug alternatives is presented below in Table 2, showing their net, positive and negative outranking flow values.

Table 2 : Complete Ranking of Alternative Migraine Drug

Rank	Alternatives	Phi	Phi+	Phi-
1	Pizotifen	0,4781	0,5566	0,0785
2	Naratriptan	0,1934	0,3846	0,1912
3	naproxen	0,1652	0,4164	0,2512
4	Diclofenac	0,1487	0,3908	0,2421
5	Rizatriptan	0,1221	0,3527	0,2306
6	metoclopramide	0,1040	0,3402	0,2362
7	Frovatriptan	0,0857	0,3724	0,2867
8	Zolmitriptan	0,0744	0,3246	0,2502
9	Nadolol	0,0264	0,3283	0,3019
10	Aspirin	0,0245	0,2845	0,2600
11	Paracetamol	0,0205	0,2977	0,2771
12	Botulinum-toxin	0,0138	0,2971	0,2833
13	Almotriptan	0,0109	0,3090	0,2981
14	Domperidone	-0,0056	0,2817	0,2874

15	Flurbioprofen	-0,0174	0,2960	0,3135
16	Ergotamine	-0,0468	0,2749	0,3217
17	Timolol	-0,0483	0,2504	0,2987
18	Eletriptan	-0,0572	0,2636	0,3208
19	Atenolol	-0,1578	0,2244	0,3822
20	Excedrin Migrain	-0,1663	0,1968	0,3631
21	Propranolol	-0,1782	0,2055	0,3837
22	Metoprolol	-0,1985	0,1950	0,3935
23	Ibuprofen	-0,2280	0,2240	0,4519
24	Sumatriptan	-0,3635	0,1295	0,4930

Below are illustrations of each of alternative migraine drugs showing their individual action profile of good performance points and weak performance points? Figure 9 provides the action profile of good performance points and weak performance points of Aspirin. Aspirin has good performance points in efficacy, cost, absorption, and side effect. While the weak performance points are number of tablet, half-life, dose frequency, and drug to drug interaction.

Aspirin

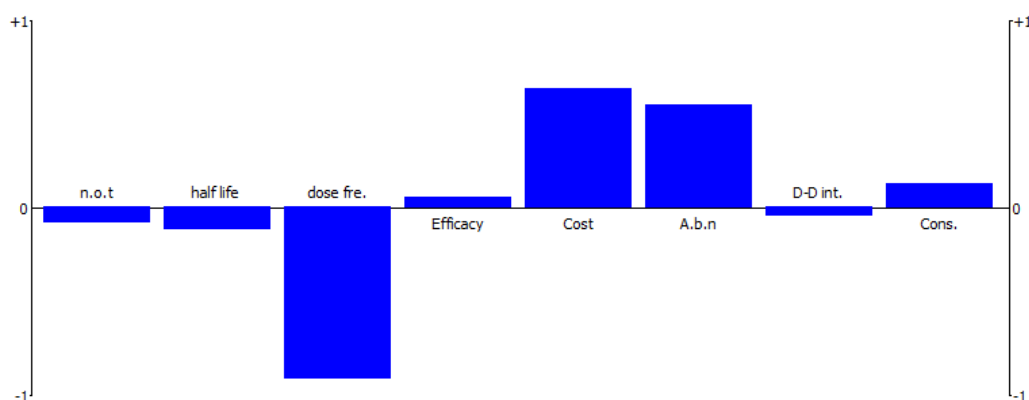


Figure 9: Action profile for aspirin showing its strong and weak points

In regards to paracetamol, the action profile shown in figure 9.1 shows efficacy, cost, absorption, drug to drug interaction, and concentration in the good performance points. In the weak performance points, number of tablet, half-life, and dose frequency are present.

Paracetamol

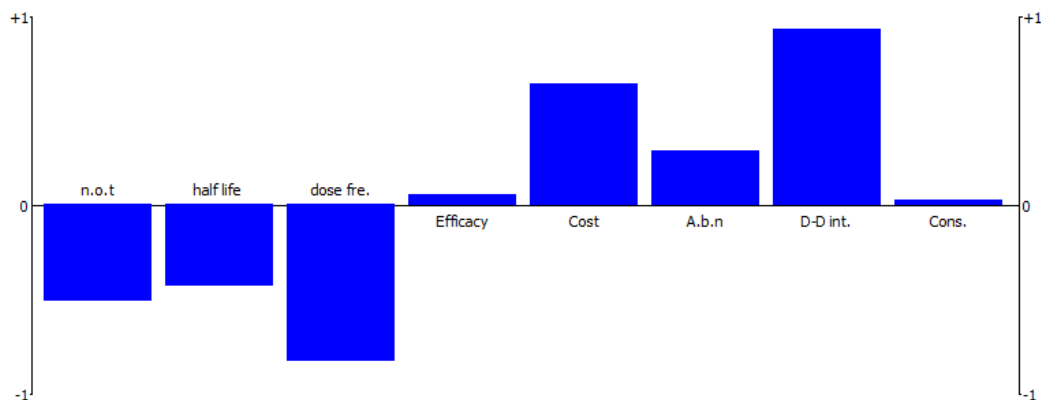


Figure 9. 1: Action Profile for Paracetamol showing its strong and weak points

Figure 9.2 present the action profile of diclofenac showing the action profile. It can be seen that it has negative outranking flow in terms of drug to drug interaction, however, it has most of its parameter in the positive outranking flow including number of tablet, half-life, dose frequency, efficacy, cost, absorption, and concentration.

Diclofenac

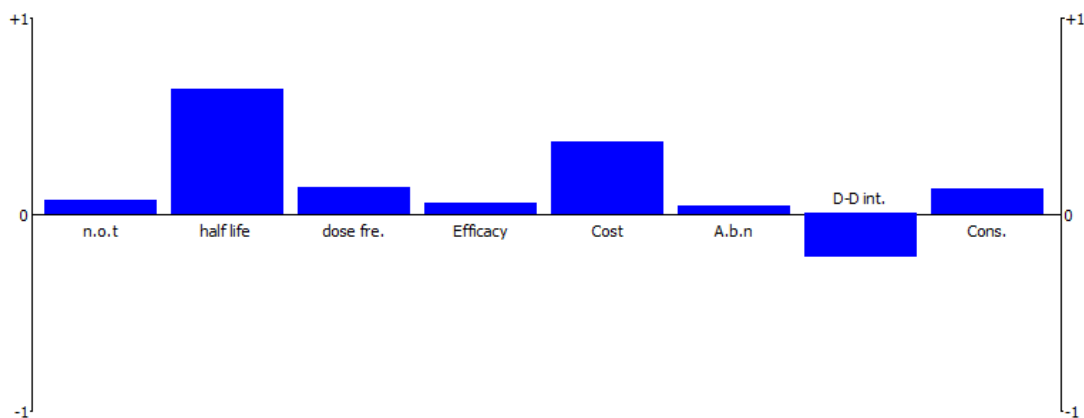


Figure 9. 2 : Action Profile for Diclofenac showing its strong and weak points

Figure 9.3 provides the action profile of good performance points and weak performance points of Excedrin migrain. Excedrin migrain has good performance points in cost and number of tablet with very promising cost effectiveness. While the weak performance points are half-life, dose frequency, efficacy, absorption, concentration and drug to drug interaction.

Excedrin migrain

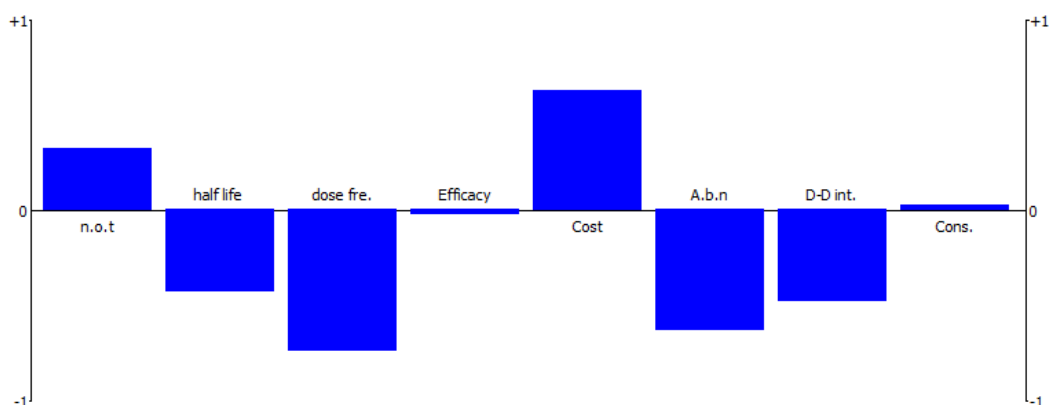


Figure 9. 3 : Action Profile for Excedrin migrain showing its strong and weak points

Figure 9.4 shows that flurbiprofen in terms of number of tablet, drug to drug interaction and concentration are in the positive outranking flow which is an indication for strong action profile of performance. However, flurbiprofen showed weak action performance in terms of half-life and dose frequency. Efficacy is situated in the net flow line

Flurbiprofen

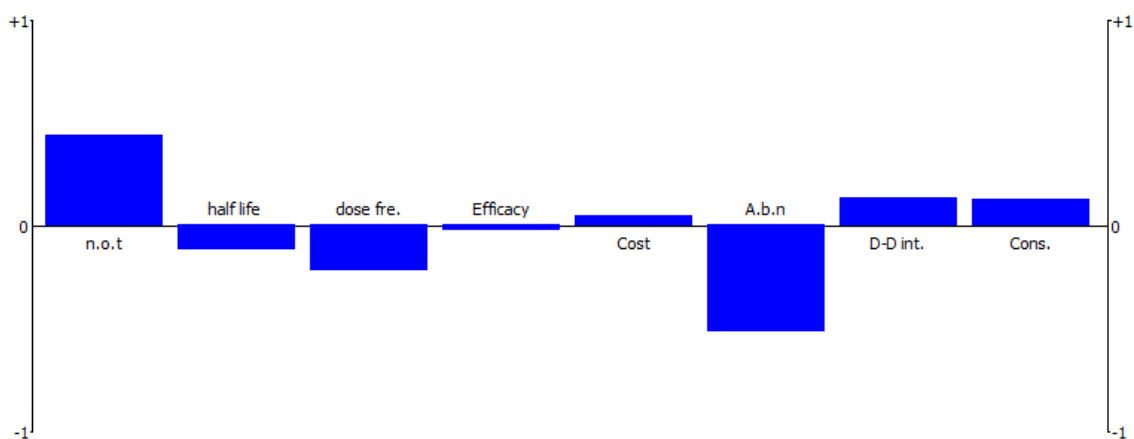


Figure 9. 4 : Action Profile for Flurbiprofen showing its strong and weak points.

Figure 9.5 is an action profile for Ibuprofen drug for the treatment of migraines which shows strong action performance in terms of cost, drug to drug interaction, and concentration. On the other hand, Ibuprofen drug for the treatment of migraines is weak in terms of number of tablet, half-life, dose frequency, efficacy, and absorption.

Ibuprofen

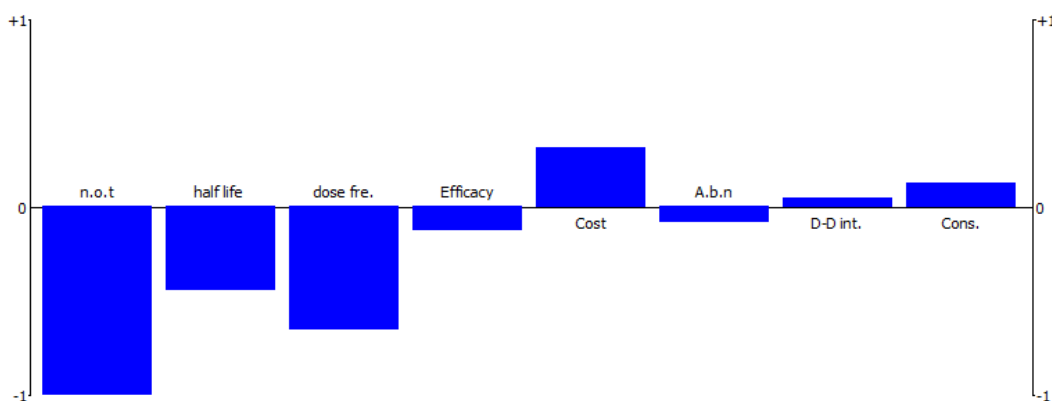


Figure 9. 5 : Action Profile for Ibuprofen showing its strong and weak points

Figure 9.6 in regards to Naproxen, the action profile shows half-life, efficacy, cost, absorption, and concentration in the good performance points. In the weak performance points, Naproxen shows number of tablet, drug to drug interaction, and dose frequency.

Naproxen

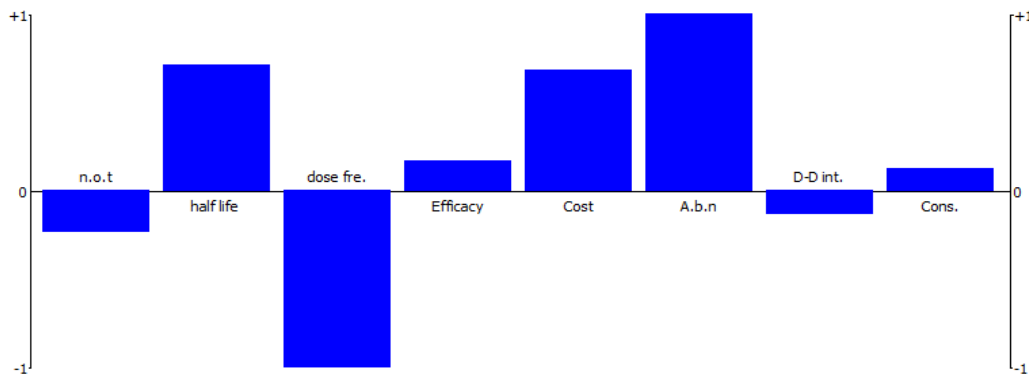


Figure 9. 6 : Action Profile for Naproxen showing its strong and weak points

In regards to Almotriptan, the action profile shown in figure 9.7 shows does frequency, absorption, drug to drug interaction and concentration are in the good performance points. In the weak performance points, Almotriptan has number of tablet, half-life, and cost with efficacy in the net flow line.

Almotriptan

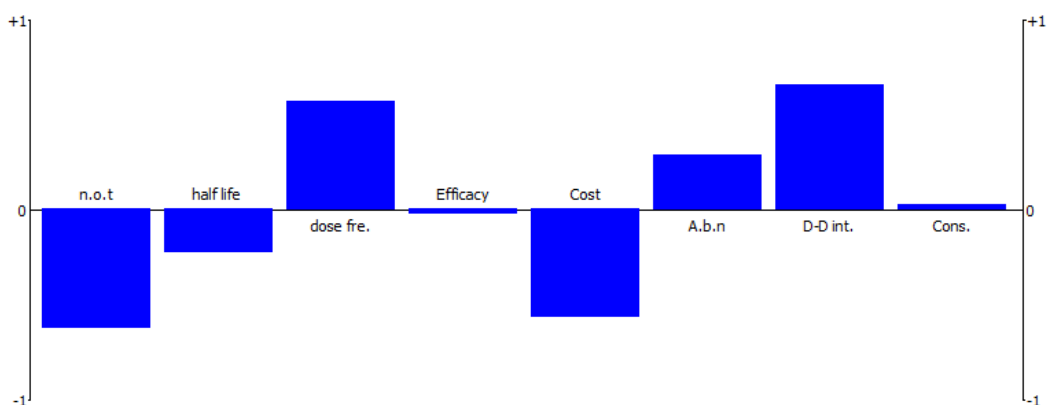


Figure 9. 7 : Action Profile for Almotriptan showing its strong and weak points

Figure 9.8 shows that Naratriptan in terms of number of tablet, dose frequency, drug to drug interaction and absorption are in the positive outranking flow which is an indication for strong action profile of performance. However, Naratriptan showed weak action performance in terms of concentration and cost. Efficacy and half-life is situated in the net flow line

Naratriptan

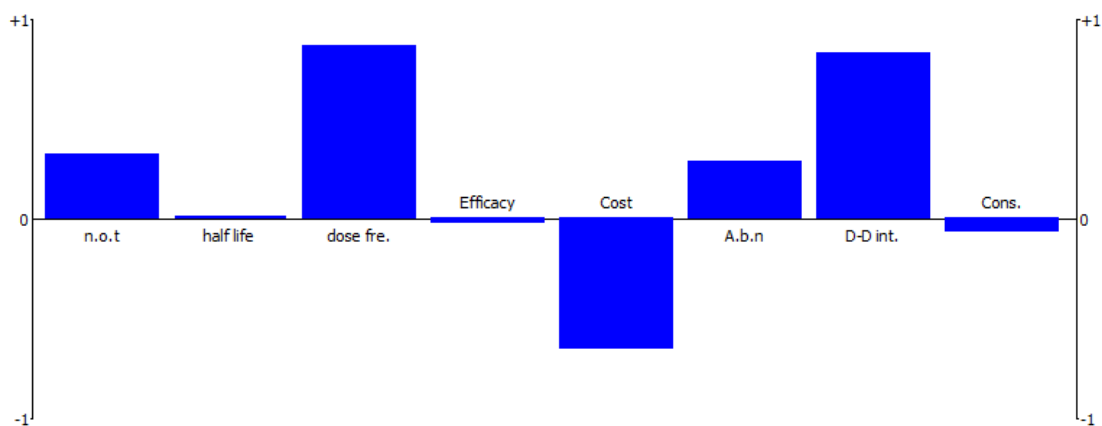


Figure 9. 8 : Action Profile for Naratriptan showing its strong and weak points

In regards to Eletriptan, the action profile shown in figure 9.9 shows number of tablet, dose frequency, absorption, and drug to drug interaction in the good performance points. In the weak performance points, Eletriptan has cost and concentration with efficacy and half-life in the net flow line.

Eletriptan

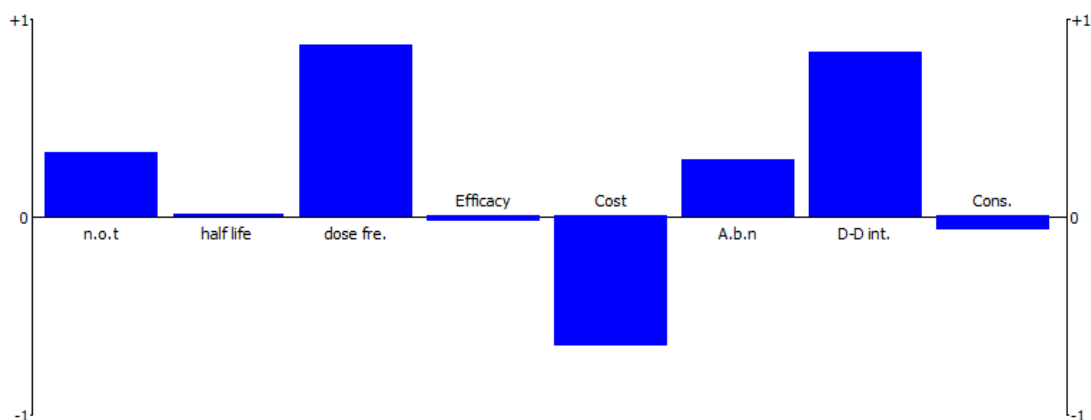


Figure 9. 9 : Action Profile for Eletriptan showing its strong and weak points

In regards to Rizatriptan, the action profile shown in figure 9.10 dose frequency, absorption, and drug to drug interaction in the good performance points. In the weak performance points, Rizatriptan has shown number of tablet, cost, half-life and concentration with efficacy in the net flow line.

Rizatriptan

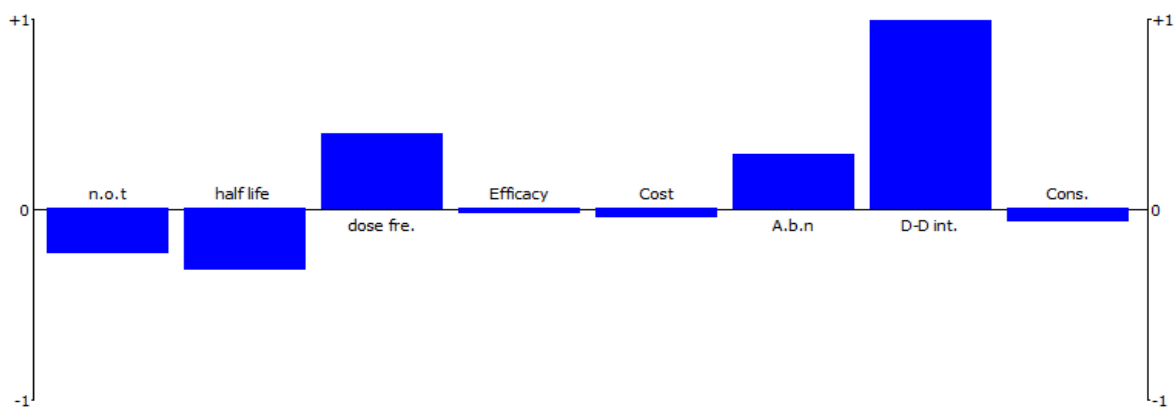


Figure 9. 10 : Action Profile for Rizatriptan showing its strong and weak points

Figure 9.11 present the action profile of Frovatriptan showing the action profile. It can be seen that it has negative outranking flow in terms of cost, absorption and concentration. However, it has most of its parameter in the positive outranking flow including drug to drug interaction, number of tablet, half-life, and dose frequency. Efficacy is found on the net flow line.

Frovatriptan

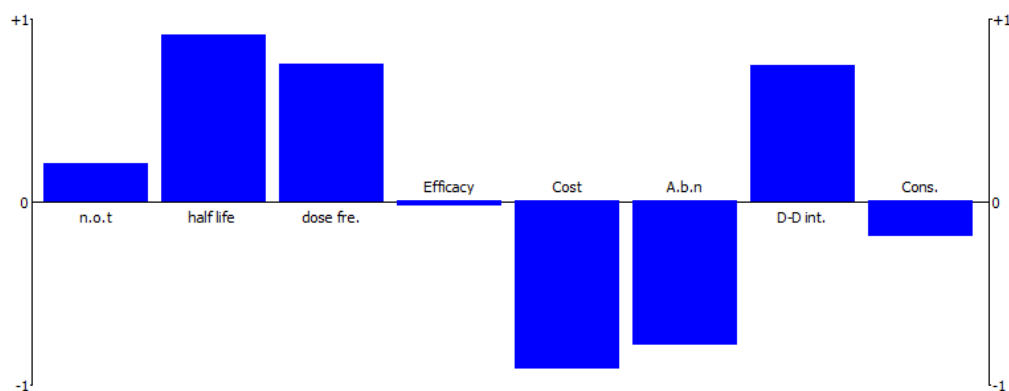


Figure 9. 11 : Action Profile for Frovatriptan showing its strong and weak points

Figure 9.12 present the action profile of Sumatriptan showing the action profile. It can be seen that it has most of its parameters in the negative outranking flow in terms of half-life, dose frequency, efficacy, cost, absorption and drug to drug interaction, however, it has only not in the positive outranking flow.

Sumatriptan

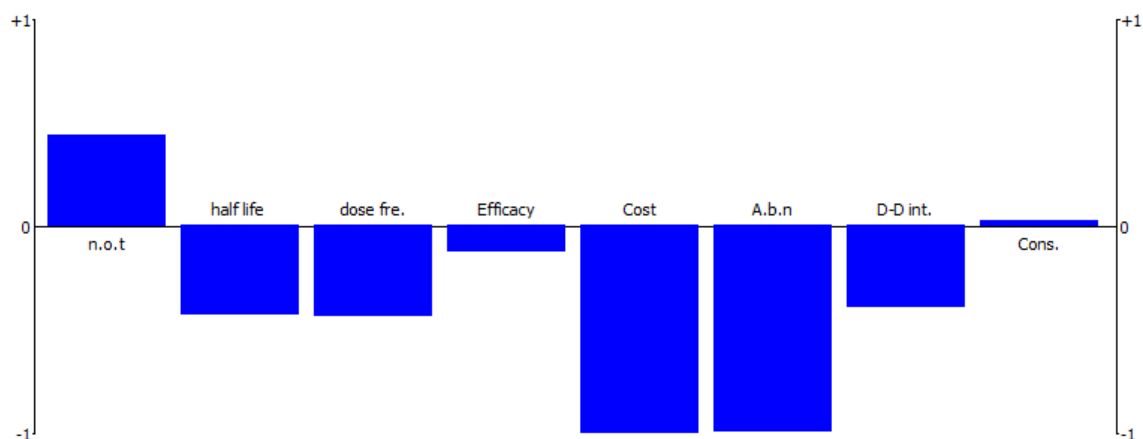


Figure 9. 12 : Action Profile for Sumatriptan showing its strong and weak points

Figure 9.13 present the action profile of Zolmitriptan. It can be seen that it has negative outranking flow in terms of number of tablet, half-life, efficacy, cost and concentration. However, it has in the positive outranking flow dose frequency, absorption, and drug to drug interaction.

Zolmitriptan

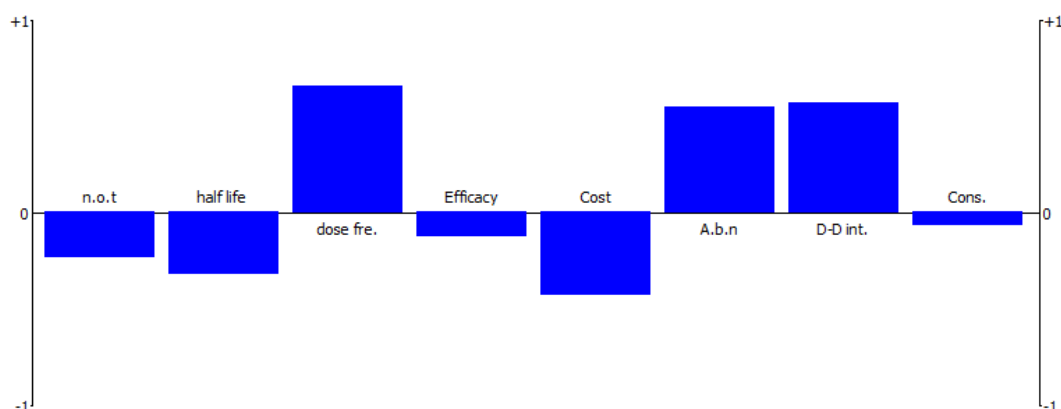


Figure 9. 13 : Action Profile for Zolmitriptan showing its strong and weak points

Figure 9.14 in regards to Ergotamine, the action profile shows number of tablet and dose frequency in the good performance points. In the weak performance points, Ergotamine shows drug to drug interaction, half-life, efficacy, cost, absorption, and concentration

Ergotamine

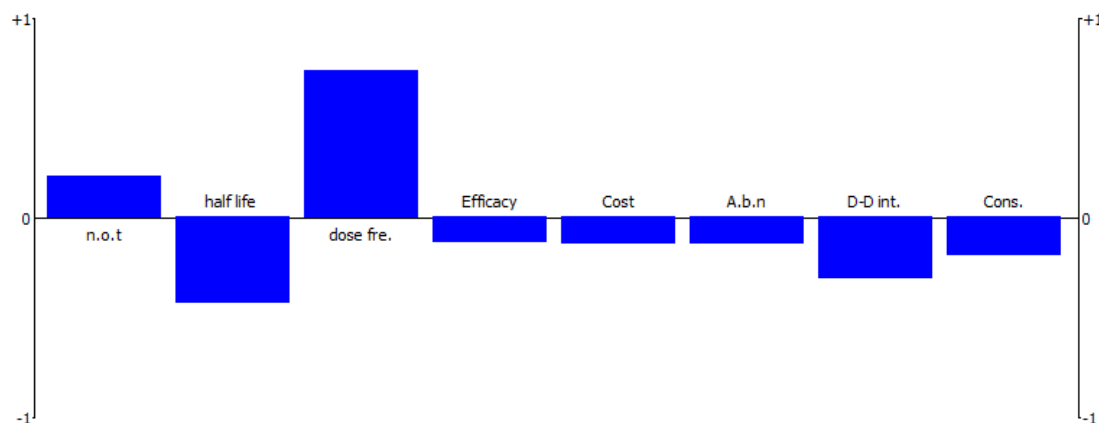


Figure 9. 14 : Action Profile for Ergotamine showing its strong and weak points

Figure 9.15 in regards to Propranolol, the action profile shows on efficacy and absorption in the good performance points. In the weak performance points, Propranolol shows number of tablet, drug to drug interaction, half-life, efficacy, cost, dose frequency, absorption, and concentration.

Propranolol

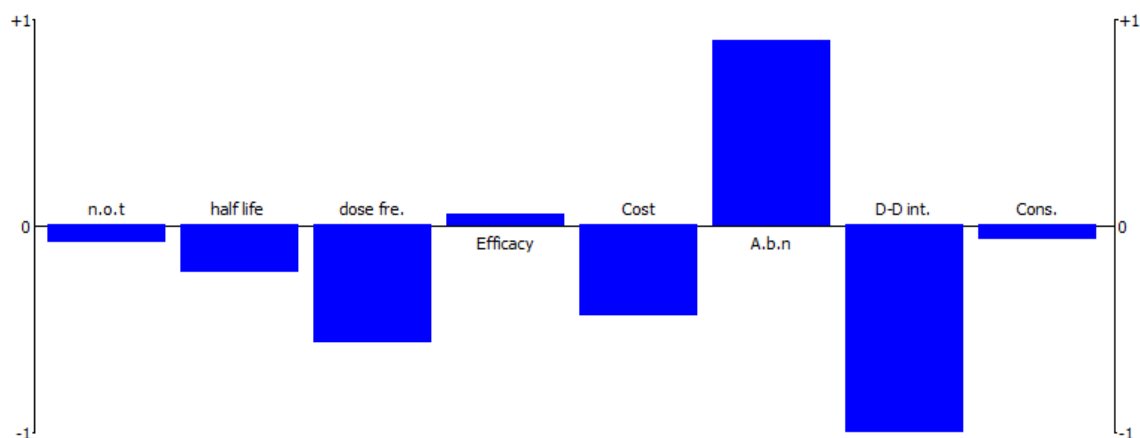


Figure 9. 15 : Action Profile for Propranolol showing its strong and weak points

In regards to Atenolol, the action profile shown in figure 9.16 number of tablet, half-life, and efficacy in the good performance points. In the weak performance points, Atenolol has shown dose frequency, cost, absorption, drug to drug interaction and concentration.

Atenolol

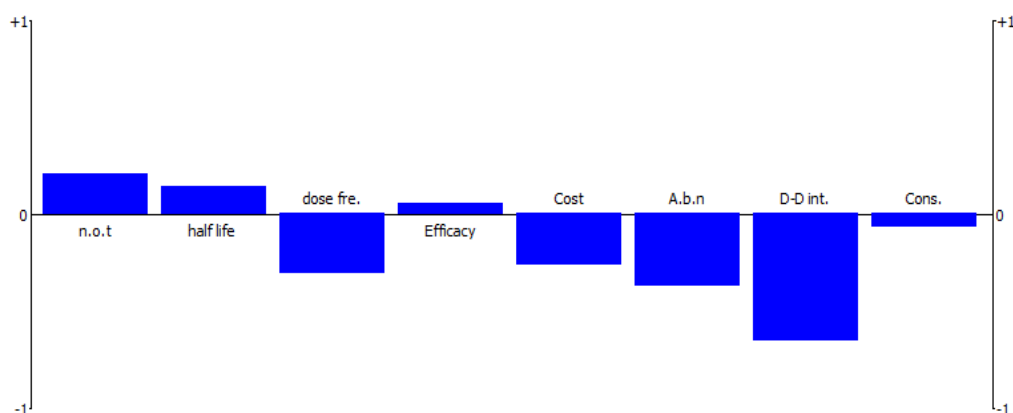


Figure 9. 16 : Action Profile for Atenolol showing its strong and weak points

In regards to Metoprolol, the action profile shown in figure 9.17 efficacy and cost in the good performance points. In the weak performance points, Metoprolol has shown dose frequency, cost, absorption, drug to drug interaction and concentration, number of tablet, half-life. Concentration is on the net flow line

Metoprolol

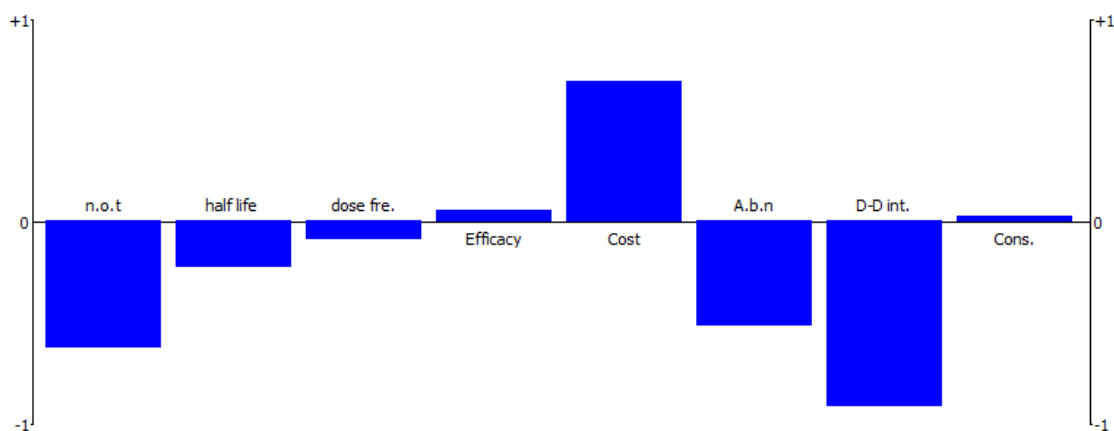


Figure 9. 17 : Action Profile for Metoprolol showing its strong and weak points

Figure 9.18 provides the action profile of good performance points and weak performance points of Nadolol. Nadolol has good performance points in cost, number of tablet, half-life, dose frequency, and efficacy. While the weak performance points are absorption, and drug to drug interaction. Concentration is in the net flow line.

Nadolol

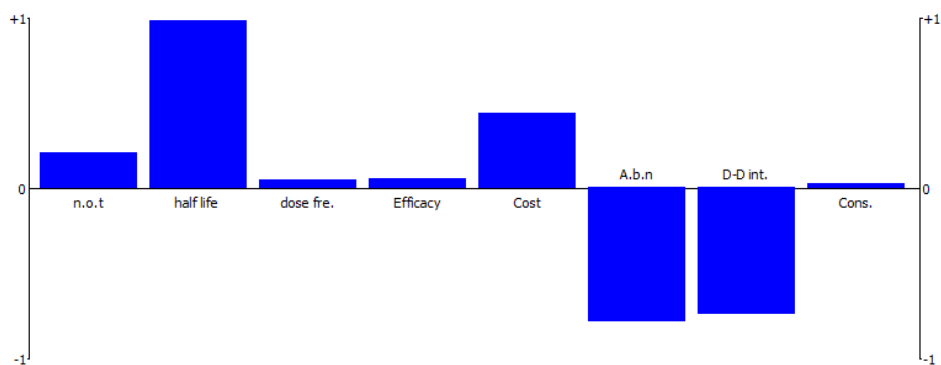


Figure 9. 18 : Action Profile for Nadolol showing its strong and weak points

Figure 9.19 provides the action profile of good performance points and weak performance points of Timolol. Timolol has good performance points in cost, dose frequency, and efficacy. While the weak performance points are absorption, number of tablet, half-life and drug to drug interaction. Concentration is in the net flow line.

Timolol

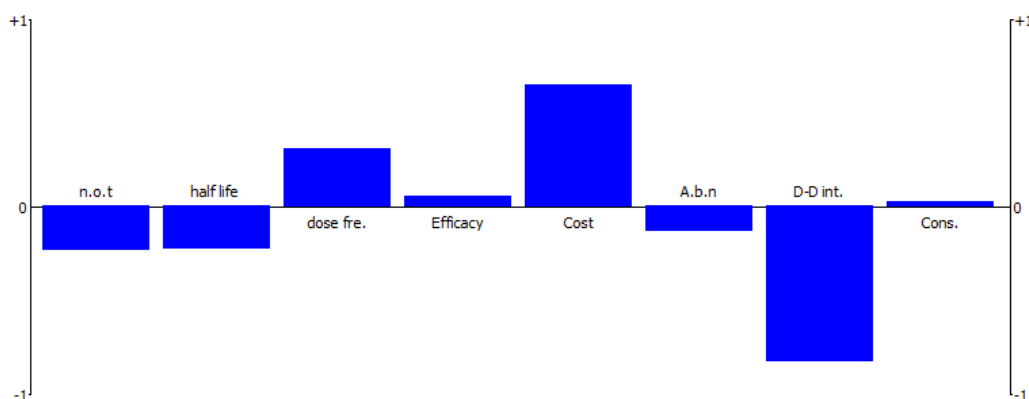


Figure 9. 19 : Action Profile for Timolol showing its strong and weak points

Figure 5.20 the high positive outranking flow value of pizotifen is because the drug shows excellent performance in terms of dose frequency, cost, half-life, a drug to drug interaction, absorption, and a number of tablet. Moreover, the low negative outranking flow value is because pizotifen was found to have poor performance in terms of efficacy and concentration Pizotifen.

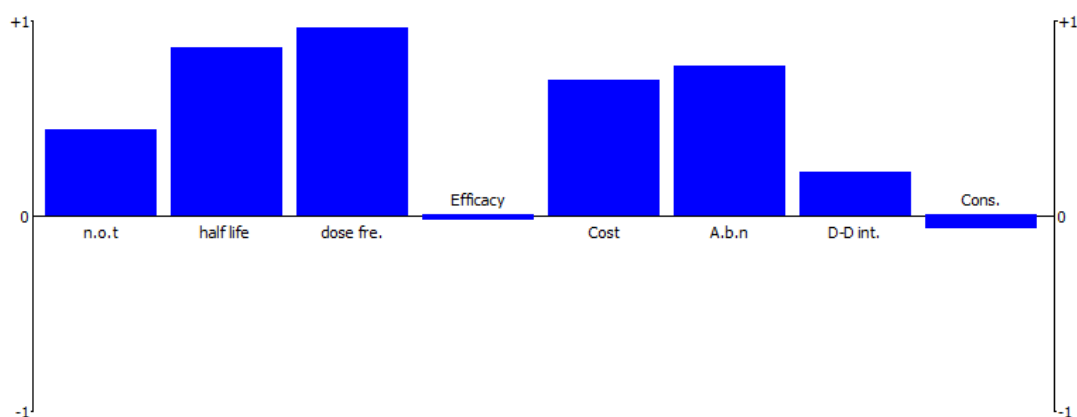


Figure 9. 20 : Action Profile for pizotifen showing its strong and weak points

In regards to Botulinum toxin type A, the action profile shown in figure 9.21 shows number of tablet, absorption drug to and drug interaction are in the good performance points. In the weak performance points, Botulinum toxin type A has half-life, and cost dose frequency, and concentration with efficacy in the net flow line.

Botulinum toxin type A

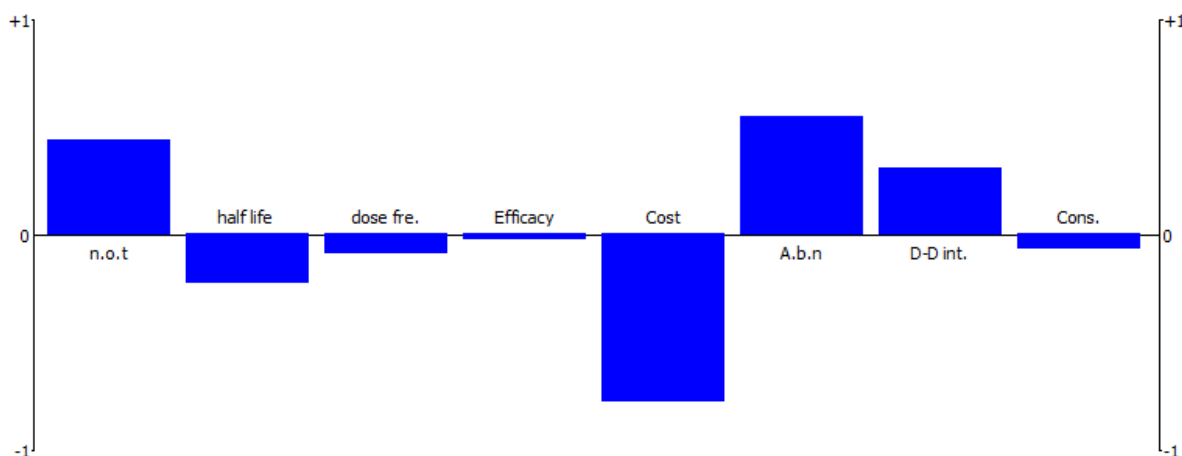


Figure 9. 21 : Action Profile for Botulinum toxin type a showing its strong and weak points

In regards to Metoclopramide, the action profile shown in figure 9.22 shows does frequency, number of tablet, absorption, and concentration are in the good performance points. In the weak performance points, Metoclopramide has drug to drug interaction and cost with efficacy and half-life in the net flow line.

Metoclopramide

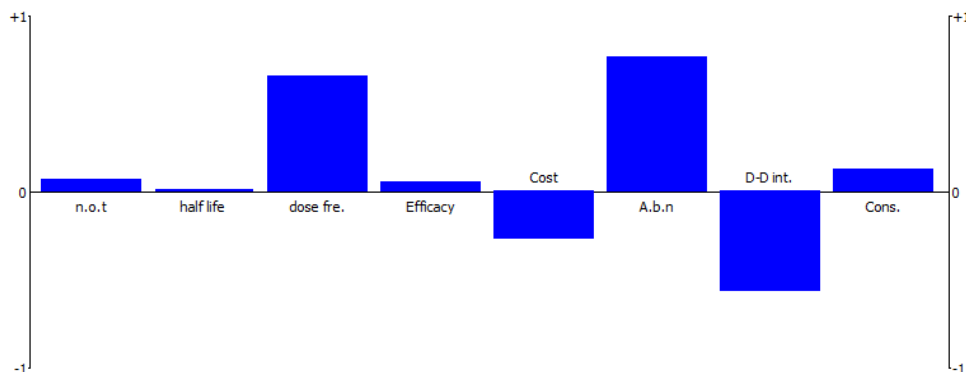


Figure 9. 22 : Action Profile for Metoclopramide showing its strong and weak points

Figure 9.23 shows the action profile of Domperidone indicating parameters including number of tablet, half-life, efficacy, cost, and drug to drug interaction in the positive outranking flow indicating strong performance. On the other hands, the parameters including dose frequency and absorption on the negative outranking flow with concertation on the net flow line.

Domperidone

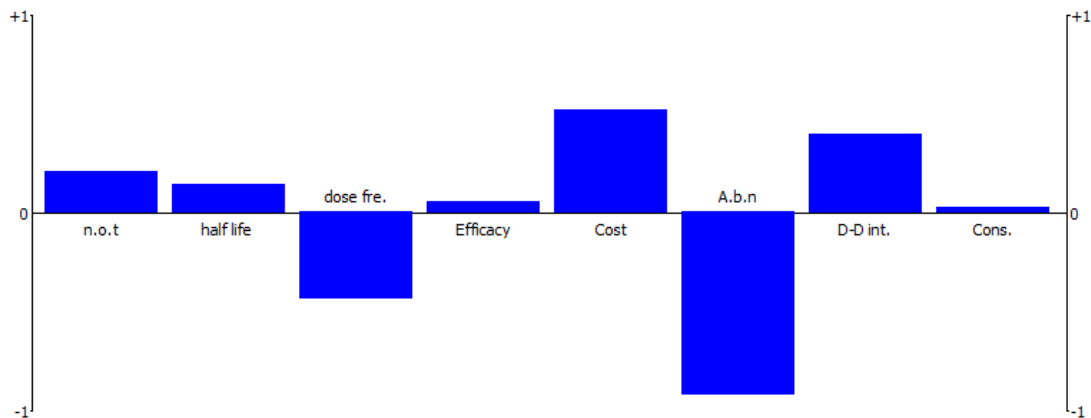


Figure 9. 23 : Action Profile for Domperidone showing its strong and weak points

Figure 9.24 shows a comprehensive summary showing the positive and negative outranking flow of each criteria (each alternative migraine drug) indicating their strong (positive outranking flow) and weak performance points (negative outranking flow). This network view can be used to clearly outline how the alternative migraine drug are ranked and the order in which they can be undertaken, from the most favorable, to the least favorable in terms of the provided parameters analyzed under the same conditions.

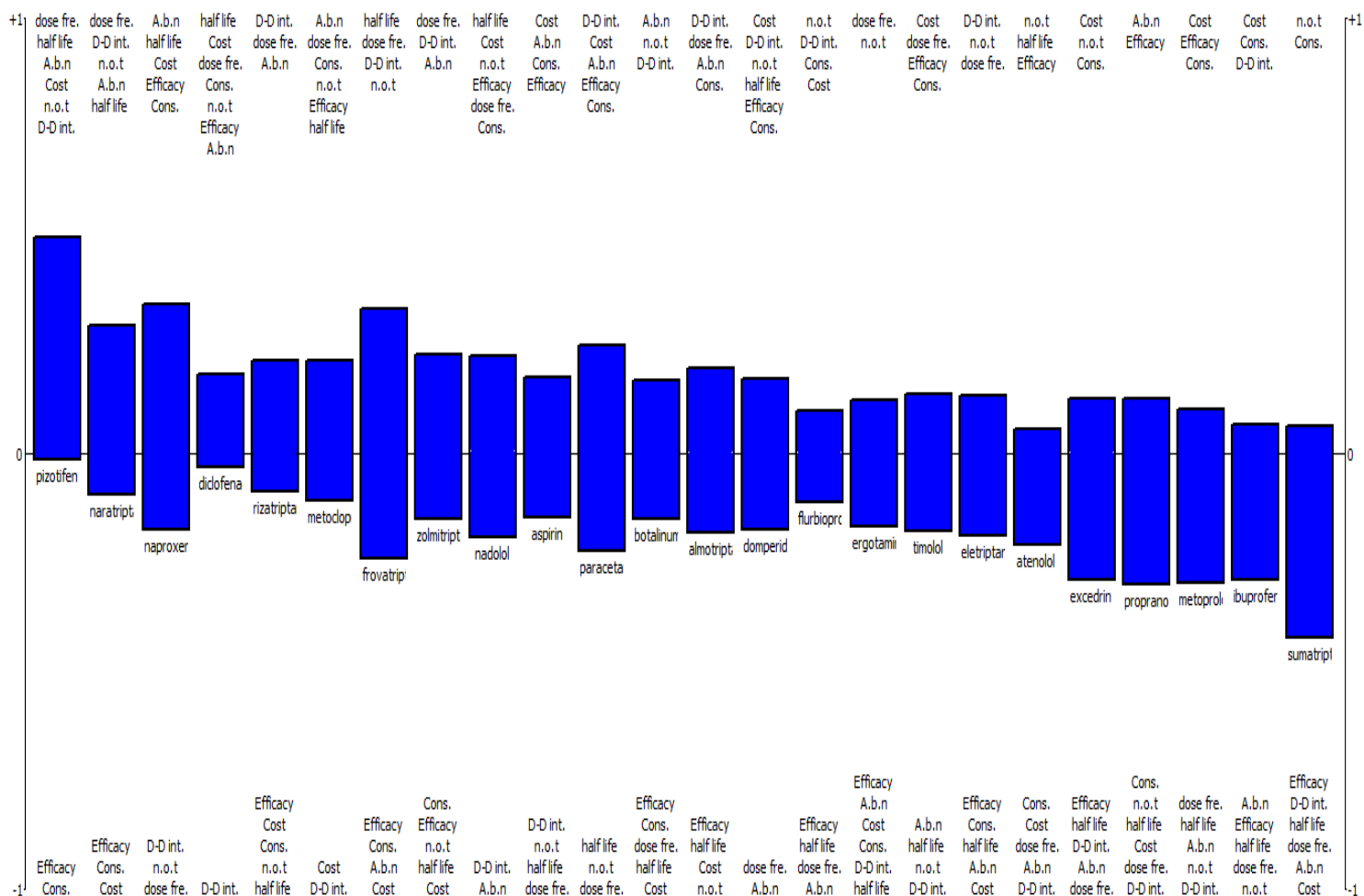


Figure 9. 24 : Rainbow Ranking of Alternative Migraine Drugs

CHAPTER 6

DISCUSSION AND CONCLUSION

This chapter provides an explanation to the findings obtained from the analysis of alternative migraine drugs in regards to their parameters as presented in chapter 5.

Discussion

From the findings of the comparative analysis of alternative migraine drugs, pizotifen was ranked the best alternative migraine drug with the highest positive outranking flow of 0,5566 and the lowest negative outranking flow of 0,0785. The high positive outranking flow value of pizotifen is because the drug shows excellent performance in terms of dose frequency, cost, half-life, drug to drug interaction, absorption, and number of tablet. Moreover, the low negative outranking flow value is because pizotifen was found to have poor performance in terms of efficacy and concentration. On the other hand, the migraine drug, sumatriptan was ranked the worst alternative migraine drug among the list of drugs considered in this study under the parameters. Sumatriptan had the lowest positive outranking flow value of 0,1295 and the highest negative outranking flow of 0,4930. The reason for the low positive outranking flow value is because sumatriptan showed good performance in only number of tablet and side effect in very low degree whereas, the reason for very high negative outranking flow value of sumatriptan is because the drug has poor performance in efficacy conc, drug to drug interaction, half-life, dose frequency, absorption, and cost in high degrees. Previous studies have successfully applied the concept of fuzzy PROMETHEE to effectively compare alternative criteria that share the same parameters. This thesis has verified the user friendliness of this concept and the effectiveness of the fuzzy PROMETHEE method as it has effectively compared 24 selected alternative migraine drugs in regards to vital parameters considered in the treatment of migraines.

It is important to note that the ranking may differ base on the weighing of the parameters in such a way that it effectively ranks the alternative drugs based on the user's weighing intentions. For this thesis, the weight used on the parameters is a generalized weight based on expert opinion of most likely and commonly seen situation of migraine and the factors considered before administering drugs. However, the weights can be changed based on the desires and health condition of the patient or the discretion of the physician in order to arrive at a different ranking that will be more suitable to the patient.

Conclusions

While this thesis has successfully achieved its aim, goals and objectives of comparing alternative migraine drugs under common parameters, however, preferential ranking methods including fuzzy PROMETHEE are generally not intended for sole diagnosis. They are designed and function to assist medical professional or other necessary decision makers in making effective decision in regards to administering drugs or other alternative treatment that may be patient specific for improved therapy. As the study from this thesis has shown, the best alternative migraine drug among all the 24 selected alternatives is pizotifen due to its excellent performance characteristics while the worst in the list is sumatriptan which is due to its low performance in regards to most of its performed characteristics. Again, this result was dependent on the generalized weight used on the parameters and the general factors considered before administering drugs. However, the weights can be changed based on the desires and health condition of the patient to achieve a more patient specific diagnosis.

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